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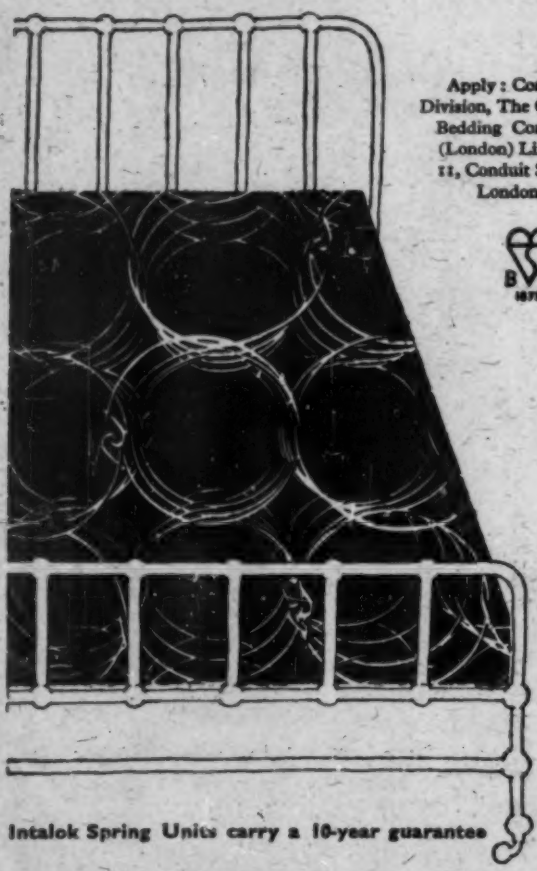

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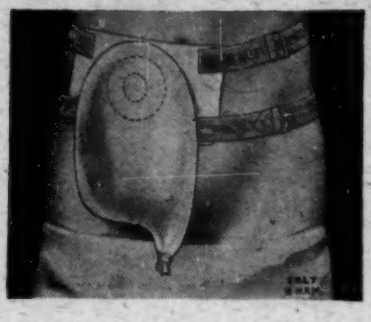

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BRITISH MEDICAL JOURNAL

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DIETARY CHOLINE AND THE MAINTENANCE OF THE CARDIOVASCULAR SYSTEM IN RATS

BY

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AND

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Professor

(From the Banting and Best Department of Medical Research, University of Toronto)

[WITH SPECIAL PLATE]

The pathological changes in the livers of a number of animal species and in the kidneys of rats resulting from an inadequate intake of lipotropic factors are well known. These effects have been extensively investigated during the two decades that have elapsed since the discovery of the lipotropic action of choline (Best and Huntsman, 1932). But the results of choline deficiency on organs other than liver and kidney have received relatively little attention. In 1945 Kesten, Salcedo, and Stetten reported cardiac necrosis in rats fed a high level of a synthetic ester of a medium-chain fatty acid (ethyl laurate, 35–40%) with a choline-deficient diet. These investigators found that choline chloride (0.35%) added to this diet completely prevented cardiac necrosis. Several years ago we noted the development of gross necrotic lesions in the hearts of choline-deficient weanling rats fed a diet containing 12% beef fat. We were uncertain of the significance of this finding and did not publish it. The report from Stetten's laboratory and our preliminary observations on cardiac necrosis in rats given *natural* fats prompted the present series of investigations.

The results have indicated that the dietary condition essential for the production of cardiac necrosis is choline deficiency *per se*. Kesten, Salcedo, and Stetten (1945) found that lesions developed only when choline deficiency was produced in rats fed ethyl laurate; other synthetic lipids did not have this effect in their experiments. Our investigations have revealed that in susceptible animals, maintained under severely hypolipotropic conditions, cardiac lesions appear when a number of different fats are used. Ethyl laurate, lauric acid, other synthetic fatty acids, and the naturally occurring fats (lard, beef fat, corn oil, and coconut oil), at levels of 25–35%, are all effective in the production of cardiac lesions in varying proportions of rats on choline-deficient diets. Even in the complete absence of dietary fat, two of thirteen rats fed a hypolipotropic diet developed significant degrees of cardiac damage.

Previous investigators (McCormick and Holman, 1949) have shown that high levels of dietary fat, in the presence of experimentally induced renal damage, are capable of producing cardiovascular lesions in dogs. Lehr and Churg (1952) produced aortic sclerosis and cardiac necrosis in rats that had developed renal injuries following the administration of sodium N-acetyl sulphathiazole. Our experiments indicate that in rats, even in the presence of apparently normal kidneys, dietary fats, inadequately balanced by lipotropic factors, may result in damage to heart and vessels. The higher the level of fat in the diet the more extensive and the more frequent are the lesions. But the production of cardiac lesions in even a small number of animals fed a fat-free choline-deficient diet emphasizes the possibility that lack of choline possesses basic aetiological significance in the production of this necrosis. High levels of dietary fat and the presence of renal damage are very important factors, but they do not appear to be the only ones essential for the production of this type of cardiac injury. There is no histological evidence suggesting any infective element in the production of these cardiovascular lesions, but the possibility cannot be completely dismissed that some such process might flourish in the absence of dietary choline.

We are unaware of any convincing evidence to indicate that hypolipotropic diets are involved in the aetiology of any type of cardiovascular disease in man. Nevertheless, the consistent production of severe cardiac injury by the removal of a naturally occurring component from a diet containing natural fats, and the prevention of this lesion by restoring the missing factor, choline, may prove to be of fundamental importance in the understanding of factors responsible for the maintenance of the cardiovascular system.

Methods

In the experiments described below 421 rats of the Wistar strain were used. In all but two groups (Table VI, groups 2 and 4) the animals were males. The average weights at the beginning of each experiment ranged from 70 to 120 g. Rats were housed in individual metal cages equipped with wire bottoms and were supplied

with fresh water at all times. The duration of the experimental periods varied from 12 to 60 days, and at the conclusion surviving animals were sacrificed under ether anaesthesia.

Diets

Five basal choline-deficient diets were employed (Table I). These varied in their physical state and protein content. The initial diet (diet A) was similar to that of Kesten, Salcedo, and Stetten (1945) and contained 35% of ethyl laurate. This diet was semi-liquid, and the food intake of rats maintained on it was low. Diet B was therefore devised to secure a more solid state by the inclusion of a large amount (15%) of cellu-flour. The food intake of animals given this diet was considerably better than those on diet A (Table II). The remaining diets (C, D, and E) contained varying amounts of protein and methionine (columns 9 and 10, Table I), and therefore differed in their lipotropic potency.

TABLE I

Diet	Casein	Alc. Ext. Peanut Meal	Alpha Soya Protein	Cystine	Cellu-flour	Salt Mixture*	Vitamin† Mixture‡	Sucrose + Fat	Protein Content g./100 g. Food Mixture	Methionine Content mg./100 g. Food
A	15	—	—	—	2	4	—	79	15	450
B	15	—	—	0·5	15	2	1	66·5	15	450
C	5	40	5	—	—	3	1	46	30	440
D	10	30	5	—	5	3	1	46	30	530
E	7	28	5	—	—	3	1	56	26	440

* The composition of the salt mixture (*Canad. J. med. Sci.*, 1953, **31**, 135) was as follows: 1 kg. contains $CaCO_3$, 110 g.; $CaHPO_4$, 325 g.; K_2HPO_4, 275 g.; $MgSO_4.3.5H_2O$, 100 g.; NaCl, 150 g.; ferric citrate, 30 g.; "trace element mixture," 10 g. The latter contains, per 100 g.: $CaCO_3$, 70 g.; $MnSO_4.4H_2O$, 19.85 g.; $ZnSO_4.7H_2O$, 3.50 g.; $CuSO_4.5H_2O$, 4 g.; KI, 0.05 g.; NaF, 0.05 g.; $Al_2(SO_4)_3.K_2SO_4.24H_2O$, 0.40 g.; $CoCl_2.6H_2O$, 0·05 g.; $Na_2SiO_3.9H_2O$, 2 g.; and $NaAsO_2$, 0.10 g.

† The composition of vitamin mixture (*Canad. J. med. Sci.*, 1953, **31**, 135) was as follows: thiamine hydrochloride, 500 mg.; riboflavine, 250 mg.; pyridoxine hydrochloride, 200 mg.; calcium pantothenate, 1 g.; nicotinic acid, 1 g.; folic acid, 50 mg.; biotin, 30 mg.; 2-methyl-1,4-naphthoquinone, 100 mg.; *p*-aminobenzoic acid, 10 g.; inositol, 50 g.; and finely powdered sucrose (100 mesh) to 1,000 g.

‡ Cod-liver oil concentrate (0.01%) and alpha-tocopherol acetate (0.015%) supplemented all diets but that used in the preliminary experiment (Expt. A). Obtained from Ayerst, McKenna, and Harrison, Ltd., Montreal; contains 200,000 I.U. vitamin A and 50,000 I.U. vitamin D per g.

Methods of Gross and Microscopical Examination

Complete necropsies were performed on all rats. Frequently, fatty and necrotic areas could be seen on gross examination of the hearts. With a minimum of delay, blocks of tissue were removed and trimmed to a thickness not greater than 0.5 cm. and immersed in either 10% commercial formalin diluted in 5% calcium chloride in distilled water (for frozen sectioning), or in Bouin's mixture prepared with picric and trichloracetic acids (for paraffin sectioning). During fixation (a minimum period of 8–12 hours) the jars containing fixative and tissues were subjected to continuous gentle agitation by a machine devised in our laboratory. Dehydration of Bouin-fixed blocks was accomplished in multiple changes of absolute isopropyl alcohol, using an automatic machine. Paraffin sections were cut in the usual manner and stained routinely with haematoxylin and eosin. Selected blocks were specially treated to demonstrate myofibrils, connective tissue, etc. Tissues so studied included heart, aorta, kidney, liver, diaphragm, skeletal muscle, lungs, pancreas, and adrenals. Frozen sections of the blocks of hearts fixed in formol–calcium mixture were cut, and were stained to demonstrate fat by Wilson's modification of Lillie's supersaturated isopropyl method, employing oil red O (Wilson, 1950). Histochemical tests for phospholipids (Baker, 1945) and cholesterol were carried out. Both phase microscopy and the polarizing microscope were used in examining many of the sections.

Results

The results of the various experiments are reported in the series of tables (Tables II–VI), in which the details of the basal diet and the content and type of fat are listed. The first group of experiments was designed after those of Kesten, Salcedo, and Stetten (1945). A series of synthetic fatty acids was then tested under similar conditions and the hearts of the experimental animals were examined. Finally, studies were made of hearts of rats that had been fed naturally occurring fats with choline-deficient rations.

Ethyl Laurate

In the initial experiment (Table II), employing Kesten, Salcedo, and Stettens's original diet (diet A), the rats consumed only 3.1 g. a day. This low calorie intake was presumably largely responsible for the fact that 50% survived for 12 days, that the incidence of the lesions was only half that reported by the previous investigators, and that cardiac damage took twice as long to develop. Both

G. F. WILGRAM ET AL.: LEGENDS TO PLATE

FIG. 1.—Heart of a young male rat which had received a choline-deficient diet containing 35% of lard. This represents an early stage in the development of cardiac damage. Stainable fat droplets are present in the right central region of the photomicrograph. The encircled area is enlarged in upper left inset. Fat droplets appear black in the picture. Frozen section stained by Wilson's technique. Wratten B and G filters. (×100 and ×400.)

FIG. 2.—Heart of a young rat fed a choline-deficient diet containing 35% of lard. This photomicrograph represents a later stage in the development of cardiac damage than that illustrated in Fig. 1. Swollen muscle fibres which contain stainable fat droplets (black) are undergoing early necrosis and lysis. In the centre and upper left are macrophages containing fat droplets. A few fat droplets appear to lie free in the interstitial space. Frozen section stained by Wilson's technique. Wratten B and G filters. (×500.)

FIG. 3.—Heart of a young rat fed a choline-deficient diet containing 35% of beef fat. This illustrates an advanced stage of cardiac necrosis. Note destruction of muscle fibres and replacement by cellular debris, macrophages, and inflammatory cells. Paraffin section stained with phosphotungstic acid haematoxylin. Wratten B and G filters. (×200.)

FIG. 4.—Higher magnification of heart illustrated in Fig. 3. This demonstrates various stages of necrosis and lysis of heart-muscle cells. (×600.)

FIG. 5.—A focus of cardiac necrosis in a rat fed a choline-deficient diet containing 35% of lard is illustrated. This focus shows several stages in the development of the lesion. Where it is most advanced in the centre, lysis of muscle fibres has occurred, with the result that fat in this region is not prominent. At the periphery of the lesion, muscle fibres, which although necrotic have not yet become lysed, contain stainable fat (black). If all portions of the lesion had been as advanced as at the centre, stainable fat would not have been observed. Frozen section stained by Wilson's technique. Wratten B and G filters. (×100.)

FIG. 6.—A portion of a papillary muscle from the heart of a choline-deficient rat fed 35% of lard is illustrated. This field demonstrates the destruction of individual muscle fibres and their replacement by a few macrophages and surviving stroma. Phosphotungstic acid haematoxylin stain. Wratten B and G filters. (×400.)

FIG. 7.—An early stage in the resolution of a focal area of cardiac necrosis in a choline-deficient rat. Macrophages and inflammatory cells have largely disappeared and the damaged muscle cells have been replaced by a loosely woven areolar stroma. Haematoxylin and eosin stain. Wratten B and G filters. (×500.)

FIG. 8.—A later stage in the resolution of an area of cardiac damage induced by dietary choline deficiency in a rat. The damaged muscle cells have now been replaced by young fibroblasts. Haematoxylin and eosin stain. Wratten B and G filters. (×400.)

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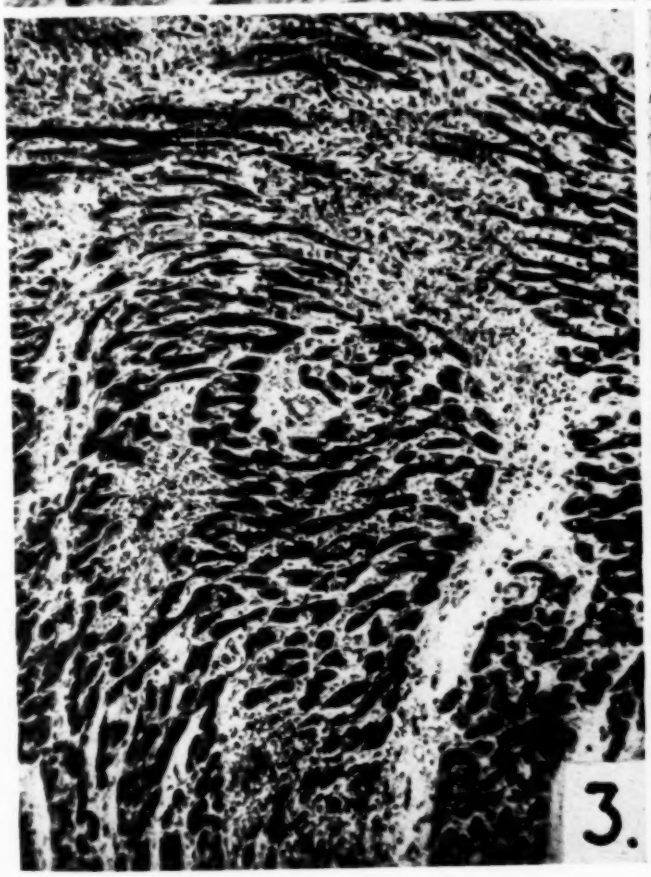
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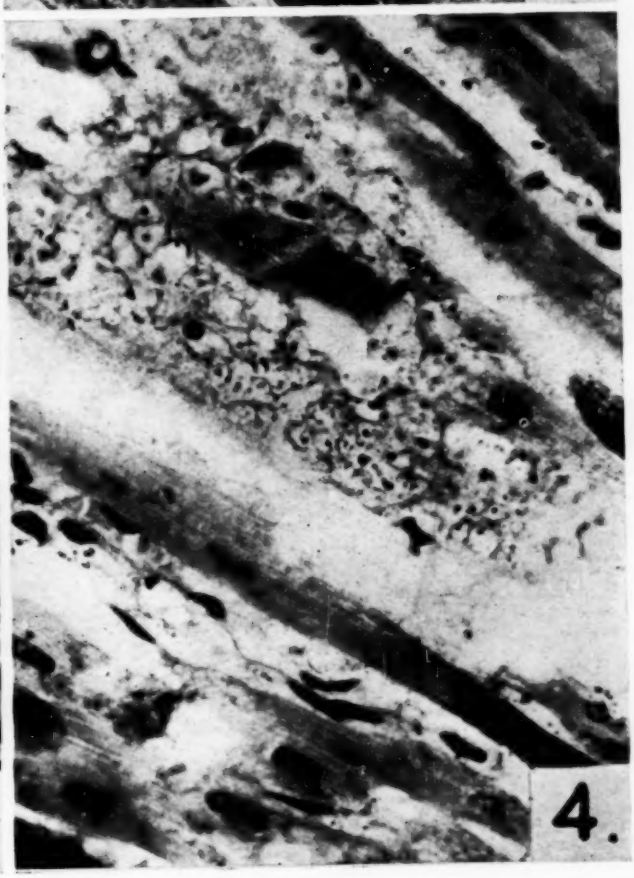
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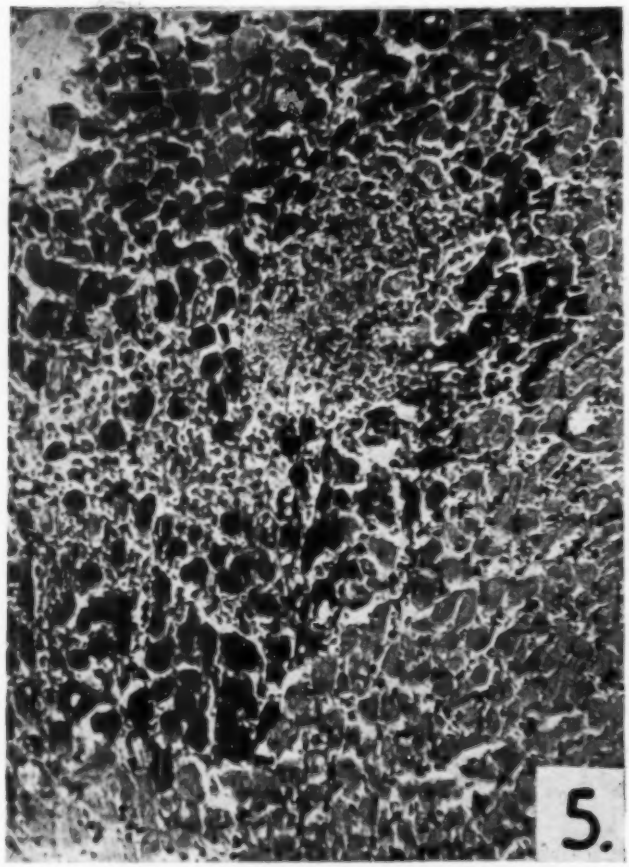
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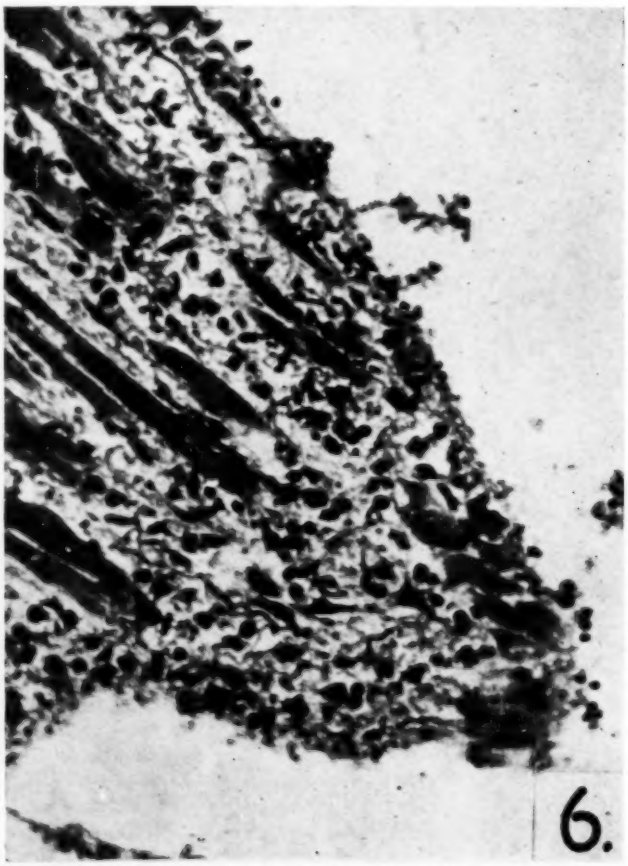
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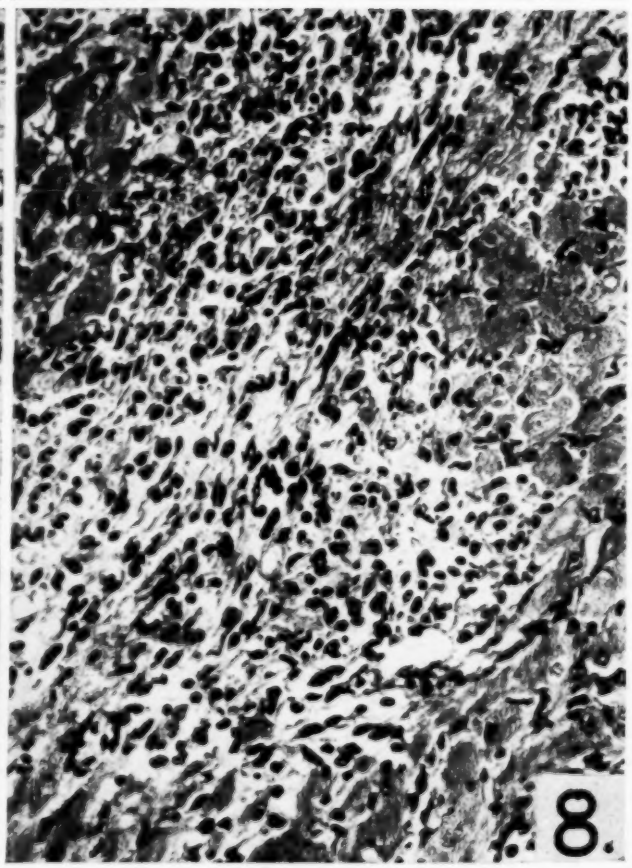
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WILLIAM M. DAVIDSON AND D. ROBERTSON SMITH: SEX DIFFERENCE IN POLYMORPHONUCLEAR LEUCOCYTES

FIG. 1.—The characteristic drumstick found in the female neutrophil leucocyte. The thin strand of chromatin joining the head to a nuclear lobe can be seen clearly. (Jenner–Giemsa. ×1,750.)

FIG. 2.—A female neutrophil showing a bilobed nucleus. Projecting from the left lobe is a characteristic drumstick, and immediately to its right, connecting the two lobes, is a minor lobe. Two trivial projections from the right main lobe are "small clubs." (Jenner–Giemsa. ×1,750.)

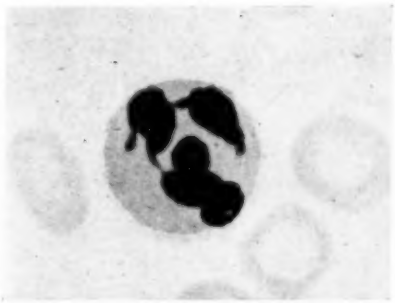


FIG. 3.—A male neutrophil. From the middle lobe a "small club" projects downwards. (Jenner–Giemsa. ×1,750.)

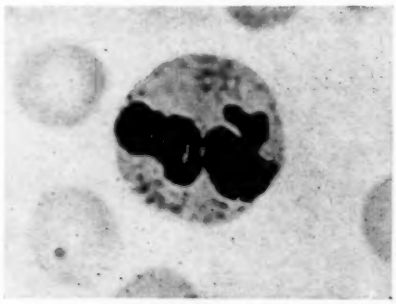


FIG. 4.—A bilobed female neutrophil. The right lobe is constricted, and from the smaller mass a chromatin-rich sessile nodule projects to the left. (Jenner–Giemsa. ×1,750.)

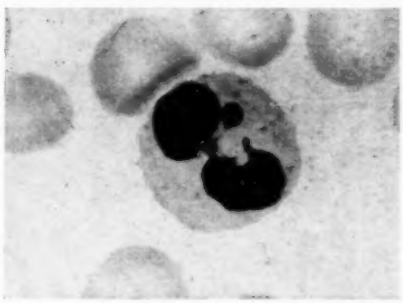
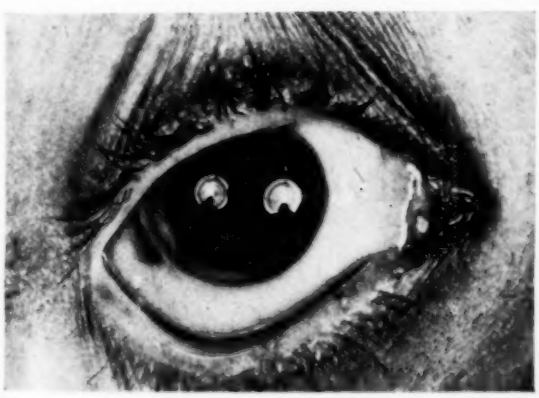


FIG. 5.—A bilobed male neutrophil with one of the rare "racket" structures between the lobes. The head of the racket has a rim of chromatin around a pale centre. (Jenner–Giemsa. ×1,750.)

D. P. NORTH: TREATMENT OF INTERSTITIAL KERATITIS

FIGS. 1 and 2.—Eyes of Case 1 before treatment with cortisone.



FIGS. 3 and 4.—Eyes of Case 1 on conclusion of therapy.

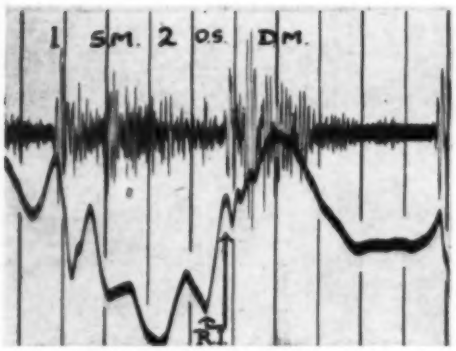


FIG. 1

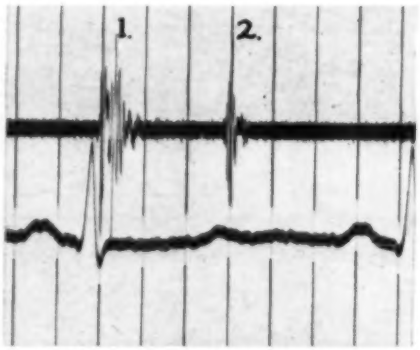


FIG. 2

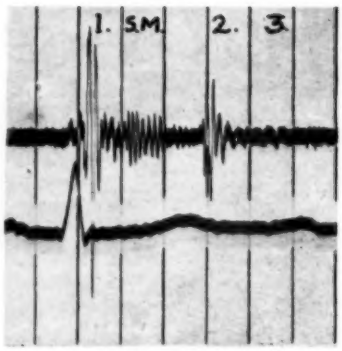


FIG. 3

FIG. 1.—Upper tracing logarithmic P.C.G. at apex. Lower tracing linear P.C.G. ("apex cardiogram"). Time lines, 0.1 sec. The patient has mitral stenosis and slight regurgitation. 1=First heart sound. 2=Second heart sound. S.M.=Systolic murmur. O.S.=Opening snap of the mitral valve. D.M.=Diastolic murmur. R.I.=Rapid inflow wave of the apex cardiogram. FIG. 2.—Normal P.C.G. in an adult, showing the first and second heart sounds. FIG. 3.—Functional ("innocent") murmur.

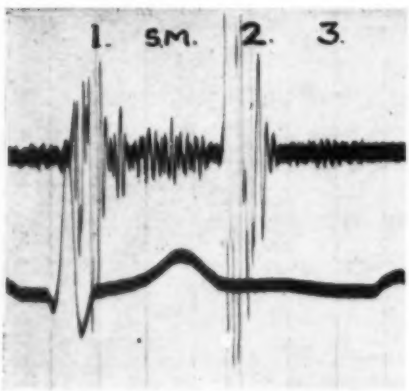


FIG. 4.—Functional ("innocent") murmur.

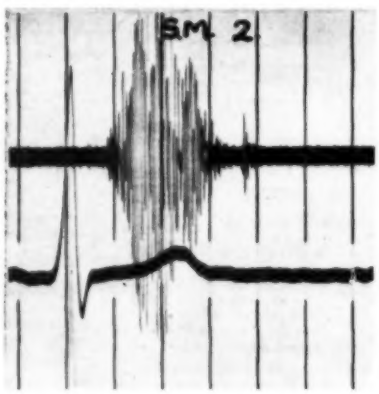


FIG. 5.—Aortic stenosis.

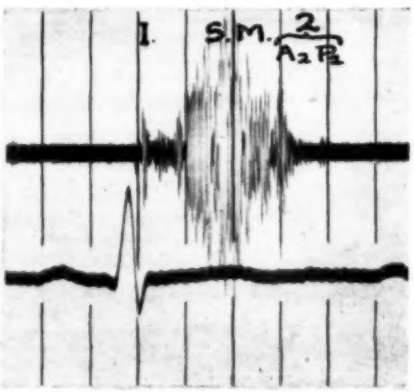


FIG. 6.—Pulmonary stenosis.

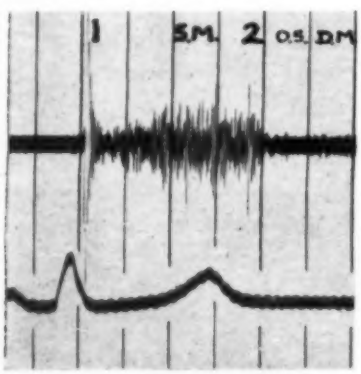


FIG. 7.—Mitral regurgitation.

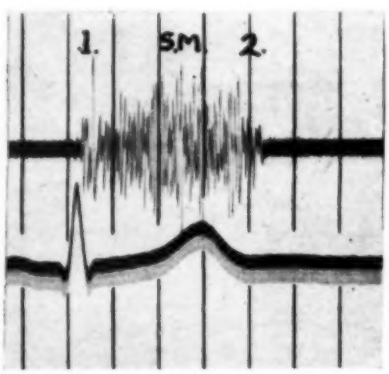


FIG. 8.—Ventricular septal defect.

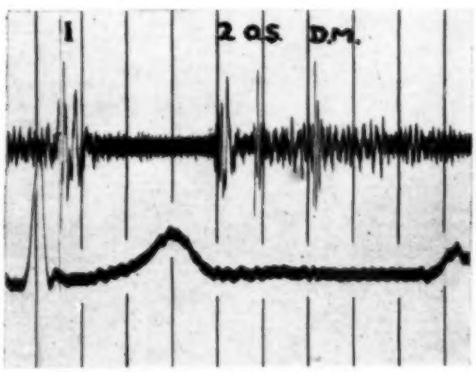


FIG. 9.—Mitral stenosis.

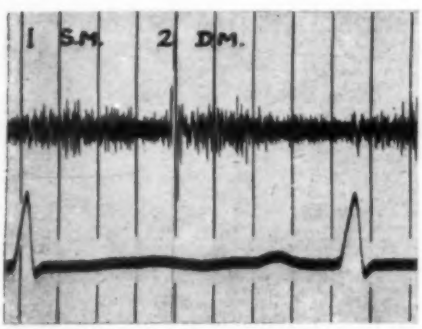


FIG. 10.—Aortic regurgitation.

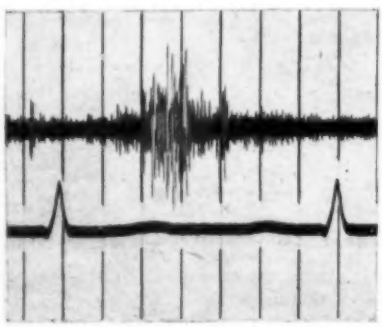


FIG. 11.—Persistent ductus arteriosus.

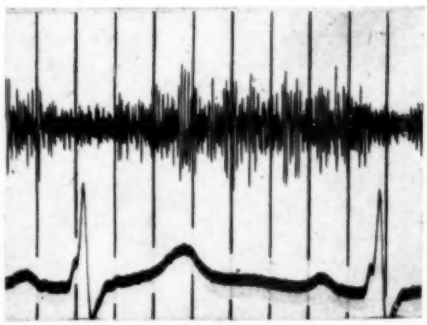


FIG. 12.—Rupture of the sinus of Valsalva into the right ventricle.

TABLE II.—*Ethyl Laurate Experiment*

Av. Initial Wt. (g.)	Diet	% Fat in Diet	Choline Chloride	Food Intake	No. of Animals	No. of Deaths Within 12 Days	Lipo-cardiosis	Cardio-necrosis
70	A	35	0	3·1	20	12	3	10
70	A	35	0·5	3·9	10	2	1	1
85	B	40	0	4·9	5	5	4	5
85	B	40	0·5	5·1	5	1	1	1

TABLE III

Av. Initial Wt. (g.)	Diet	Type of Fat	% of Fat	Choline Chloride	Food Intake	No. of Animals	No. of Deaths Within 12 Days	Lipo-cardiosis	Cardio-necrosis
85	B	Tributyrin	40	0	4·1	5	1	0	0
65	C	,,	25	0	4·5	7	2	0	0
85	B	,,	40	0·5	4·3	3	2	0	0
85	B	Tricaproin	40	0	4·1	5	4	2	2
65	C	,,	25	0	4·4	8	2	2	4
85	B	,,	40	0·5	4·6	2	0	0	0
85	B	Tricaprylin	40	0	4·5	5	3	4	3
65	C	,,	25	0	4·7	7	2	5	4
85	B	,,	40	0·5	4·5	2	0	0	0
85	B	Trilaurin	40	0	4·0	7	5	3	6
65	C	,,	25	0	4·7	8	2	0	3
85	B	,,	40	0·5	4·3	7	2	1	1
85	B	Trimyristin	40	0	3·9	5	1	0	1
65	C	,,	25	0	4·6	7	1	1	2
85	B	,,	40	0·5	4·2	2	0	0	0
85	B	Tripalmitin	40	0	3·5	5	5	1	1
65	C	,,	25	0	4·3	7	5	1	1
85	B	,,	40	0·5	3·7	2	2	0	0

TABLE IV

Experimental Group	Average Initial Weight in g.	Diet	Type of Fat	% of Fat	Choline Chloride	Food Intake Average, g./day	Duration of Experiment in Days	No. of Animals	No. of Survivors at End of Experiment	No. of Rats with Cardiac Lesions	% of Rats with Cardiac Lesions
1	85	B	Coconut oil	40	—	—	60	20	20	0	0
2	85	B	,, ,,	40	0·5	—	60	15	15	0	0
3	85	B	Lard	40	—	6·5	60	10	3	5	50
4	85	B	,,	12	—	6·7	60	5	5	0	0

TABLE V

Experimental Group	Average Initial Weight in g.	Diet	Type of Fat	% of Fat	Choline Chloride	Food Intake Average, g./day	Duration of Experiment in Days	No. of Animals	No of Survivors at End of Experiment	No. of Rats with Cardiac Lesions	% of Rats with Cardiac Lesions
1	65	E	Lard	35	—	6·3	14	5	0	5	100
2	65	C	,, ,,	25	—	6·7	14	37	0	24	65
3	65	C	,, ,,	25	0·5	7·4	14	20	18	2	10
4	65	C	,, ,,	12	—	7·6	14	20	1	9	45
5	65	C	,, ,,	2	—	8·6	14	10	2	3	30
6	65	C	Beef fat	25	—	6·9	14	10	1	8	80
7	65	C	Corn oil	25	—	6·4	14	10	3	4	40
8	65	C	Coconut oil	25	—	6·4	14	9	9	2	22

TABLE VI

Experimental Group	Average Initial Weight in g.	Diet	Type of Fat	% of Fat	Choline Chloride	Food Intake Average, g./day	Duration of Experiment in Days	No. of Animals	No. of Survivors at End of Experiment	No. of Rats With Cardiac Lesions	% of Rats with Cardiac Lesions
1	120	D	Lard	25	—	9·8	14	7	3	4	57
2	120	D	,,	25	—	9·2	21	24*	21	0	0
3	120	D	,,	25	—	10·5	21	23	9	15	65
4	120	D	,,	25	0·5	9·5	21	25*	25	2	8
5	120	D	,,	25	0·5	10·8	21	24	24	0	0
6	120	D	,,	0	—	11·1	21	13	9	2	15

* The asterisks denote female animals.

grossly and microscopically, however, the lesions conformed to the descriptions given by Kesten *et al., except that stainable fat was frequently present in many of the hearts.* Necrosis encountered in one of ten hearts of the choline-supplemented control animals was probably secondary to an associated bronchopneumonia.

With a smaller number of animals, the effect of ethyl laurate was again tested, this time with basal diet B. It proved more palatable, and the animals consumed appreciably more food (4.9 g. a day) than the rats in the initial experiment (3.1 g. a day). The characteristic lesions appeared in all of the five animals, and deaths occurred sooner than in the first experiment. These results confirmed the original observation of Kesten, Salcedo, and Stetten (1945), that high levels of ethyl laurate fed to young rats produced cardiac necrosis which could be prevented by choline.

Synthetic Triglycerides: (C_4, C_8, C_{10}, C_{12}, C_{14}, and C_{16}; Table III)

Kesten, Salcedo, and Stetten (1945) believed that only ethyl laurate produced cardiac damage when fed to choline-deficient male rats. The results of our experiments (Table III), however, in which 25 and 40% of synthetic triglycerides were fed in basal rations B and C, indicated that these triglycerides, with the exception of tributyrin, were all effective to a varying degree in producing cardiac necrosis in rats.

Fat-free Diets

Only one group of rats was fed a choline-deficient fat-free diet (Table VI, group 6). Of 13 animals, 2 developed focal deposits of stainable fat in heart muscle and myocardial necrosis (Plate, Fig. 7). Only 4 of these 13 animals succumbed to haemorrhagic renal lesions. This indicates that omission of fat had reduced the severity of the dietary deficiency.

Naturally Occurring Fats

These were lard, beef fat, corn oil, and coconut oil; Tables IV, V, and VI (Figs. 1 to 4). Four basal diets were employed in this series of experiments (diets B, C, D, and E). Depending on differences in initial weights of rats (column 2) and the protein content of the diets (columns 9 and 10, Table I), varying numbers of cardiac lesions were present in all groups of male rats receiving any of these naturally occurring fats, with the exception of one group fed 40% coconut oil in diet B (group 1, Table IV). In another experiment somewhat younger rats fed 25% coconut oil in the more severely hypolipotropic diet C did show an incidence of over 20% of cardiac lesions (group 8, Table VI). Lard and beef fat were more effective in producing a high incidence of cardiac changes than either coconut or corn oil. Under the conditions employed, females did not develop cardiac damage when fed 25% lard in basal diet D (Table VI, group 2). There are other examples of the greater resistance of female than of male rats to deficiency of lipotropic substances.

Necropsy Findings

Lesions in hearts and other organs were essentially similar in all animals, whether fed ethyl laurate, synthetic triglycerides, or one of the four naturally occurring fats.

Hearts

Myocardial degeneration, interstitial myocarditis, and infiltration of inflammatory cells, as well as frequent areas of focal necrosis, were found in various proportions of all male rats (see Tables IV–VI, columns 11 and 12) with the exception of those which received tributyrin (Table III, groups 1 and 2) and the one group fed 40% coconut oil in diet B (Table IV, group 1). In about one-fifth of the animals in which cardiac necrosis developed, the lesions could be observed on careful gross inspection with the aid

of a hand-lens. They consisted of small yellow areas scattered over the surface of the organ, and exhibited a waxy appearance. No consistent distribution of the lesions could be discerned, for they were found on every portion of both ventricles, including the apices, bases, and interventricular septa. Pericardial effusions were frequently associated with the necrotic lesions. In suitably treated frozen sections, stainable fat droplets were found in many of the muscle fibres (Figs. 1 and 2). These fat droplets were small and were often arranged in somewhat linear fashion, corresponding to the direction of the myocardial fibrils (Fig. 2). Fibres containing fat were nearly always swollen and their nuclei often pyknotic (Fig. 4). In areas of necrosis seen at later stages, fat liberated from lysed muscle cells could be found in macrophages and wandering cells (Fig. 2). Accordingly, the amount of stainable fat varied inversely with the severity and duration of the necrosis (Fig. 5). Details of the histological picture and the pathogenesis of the various stages, including that of early healing, will be published elsewhere (Wilgram and Hartroft, 1954). An example of early healing is shown in Figs. 7 and 8.

Livers

Centrilobular accumulation of stainable fat occurred regularly in the livers of all choline-deficient animals except those fed tributyrin (see below). Focal areas of hepatic necrosis were sometimes observed in some of the animals that received synthetic triglycerides. The distribution of the latter lesions was not consistently related to any specific portion of the hepatic lobule. Accumulation of abnormal deposits of fat had not progressed in any of the animals to the point where appreciable numbers of fatty cysts (Hartroft and Ridout, 1951) had been formed with their sequela of condensation reticulinosis (fibrosis ; cirrhosis).

Kidneys

Haemorrhagic renal lesions (Griffith and Wade, 1939) were found in the choline-deficient animals fed tricaproin and to a less extent in those fed tricaprylin. Renal damage did not develop, however, in rats fed tributyrin, ethyl laurate, trilaurine, trimyristine, tripalmitin, or coconut oil, nor in some of the animals fed lard. The presence of a high incidence of cardiac lesions in the animals fed ethyl laurate and trilaurine and the absence of demonstrable renal lesions is of special interest.

Gastro-intestinal Tract

In the rats fed tributyrin, abnormalities were limited to the gastro-intestinal tract. Gastric ulceration and haemorrhage, as reported by Kesten, Salcedo, and Stetten (1945) occurred regularly in these animals. The addition of choline to the diet was without effect on the incidence or severity of the ulceration.

Discussion

These results have confirmed the original finding of Kesten, Salcedo, and Stetten that a high level of ethyl laurate in the diet produces cardiac necrosis in young choline-deficient male rats. In agreement with these investigators it has also been demonstrated that when these diets are supplemented with choline chloride (0.5%) significant degrees of cardiac damage are prevented in pair-fed control animals. In extensions of these findings we have shown that other synthetic triglycerides and naturally occurring fats fed with choline-deficient diets result in a high incidence of cardiac damage in young male rats. The second new finding of considerable interest concerns the demonstration of stainable fat droplets within cardiac muscle which preceded or accompanied the necrotic changes. Stainable fat could almost constantly be demonstrated in frozen sections of heart muscle of our choline-deficient rats with cardiac damage (Figs. 1 and 2). The amount of fat after necrosis became well advanced was much less than in earlier stages (Fig. 5). Examination of many lesions at every stage in their development demonstrated that fat droplets were released from lysed muscle cells following rupture of cell membranes. Liberated fat became engulfed by tissue macrophages in which it could still be seen in stainable droplet form (Fig. 2). With further healing of the lesion, fat-containing macrophages became less numerous and eventually disappeared. Thus the more advanced the necrosis the less the amount of stainable fat. This may explain the findings of Kesten *et al.*, since in their experiments the lesions progressed so rapidly that they may have seen necrosis only in its late stages, when negligible amounts of fat would have been demonstrable. When these lesions are actively progressing (Fig. 5) stainable fat is present in the muscle fibres at the periphery of the focus of necrosis. In the centre of the necrotic area destruction of heart tissue is more advanced and very little fat remains. Therefore, if the lesions are not observed in the stage of pre-necrosis or very early necrosis, stainable fat may be absent.

The accumulation of abnormal deposits of stainable fat within liver and kidney tissue of choline-deficient rats has been shown to be the forerunner of more extensive destructive lesions (Hartroft and Ridout, 1951 ; Hartroft, 1948). The demonstration that lipocardiosis is a forerunner of cardiac necrosis suggests that its pathogenesis is similar to that of renal and hepatic lesions, in that abnormal accumulation of fat may initiate death of affected cells. The concept is emerging that adequate amounts of lipotropic factors are necessary in the diets of experimental animals to prevent the *harmful* accumulation of abnormal deposits of fat in not only liver but also kidney and heart. The first pathological lesion in all these organs is fatty change of the parenchyma, which can be prevented by choline. According to this concept, the definition of the term lipotropic should include the prevention of accumulation of fat not only in the liver but also in all other tissues in which similar phenomena have been demonstrated. In this laboratory, evidence is accumulating that, in the absence of adequate amounts of choline, fat is deposited in arterial walls with damaging effect (Hartroft, Ridout, Sellers, and Best, 1952). Therefore it can now be suggested that dietary choline and its precursors are necessary in rats for the maintenance of not only a healthy liver, but also of normal cardiovascular and renal systems. This view appears further justified by the finding, previously reported from this laboratory (Hartroft and Best, 1949), that brief periods of choline deficiency in early life may induce hypertension in rats several months later.

The Primary Nature of Cardiac Lesions in Choline Deficiency

The question arises whether the heart damage can be regarded as a direct effect of choline deficiency on the myocardium, or as secondary to renal lesions induced by the hypolipotropic regimen. Severe choline deficiency leads to acute renal damage in a high percentage of susceptible animals (Griffith and Wade, 1939). It is not surprising, therefore, to find a frequent association of cardiac and renal lesions, and it is not easy to decide whether or not one is directly dependent on the other. In 19 rats fed synthetic triglycerides (C_{13}, C_{14}, and C_{16}) and 6 animals fed naturally occurring fats (lard, coconut oil, and corn oil), cardiac lesions were encountered in the absence of gross or microscopic renal changes. These exceptions to the finding that the more severe the renal damage the higher the incidence and extent of cardiac injury suggest that the kidney damage is not the only essential factor. It may well be a contributing factor when it is present. Damage to myocardium in choline-deficient rats has never been observed in the absence of a fatty liver. It is possible that the hepatic and myocardial lesions may be interdependent, but we have no suggestions to make regarding pathways that might connect the two. Female rats of this particular age (120 g. body weight) were almost completely resistant to the development of cardiac damage induced by choline deficiency, just as they are similarly more resistant to the renal damage than are males.

Factors Influencing the Incidence of Cardiac Damage in Choline Deficiency

With few exceptions, supplements of dietary choline (0.50 to 0.85%) have been effective in maintaining a normal myocardium in the rats fed the diets used in these experiments. Of 117 controls given choline, these exceptions occurred in 7 rats with bronchopneumonia and pericarditis (see Tables). In these 7 animals, stainable fat and cardiac necrosis was observed, but the lesions were neither so focal in nature nor so widely distributed. They were largely limited to the subpericardial zone. The infiltrations of inflammatory cells were composed of a much higher proportion of polymorphonuclear leucocytes than were those encountered in the choline-deficient animals, in which mononuclear types of macrophages were present in greater numbers. Only after necrosis was well established (Fig. 6) did inflammatory cells constitute a feature of the lesions in the choline-deficient animals, and they were never present in appreciable numbers during the pre-necrotic stage of lipocardiosis (Fig. 1). Infection as a contributing agent in the aetiology of the cardiac lesions of the choline-deficient animals is not regarded as probable. The possibility does perhaps remain that the deficient animals might have been more susceptible to some bacterial or viral agent than were the supplemented controls.

The data presented in the various tables indicate that factors such as sex and age of rats, calorie intake, the protein content of the diet in relation to that of methionine, and the level of dietary fat, all operate to affect the incidence of the cardiac lesions in a manner comparable to their effect on hepatic and renal changes. The younger the animals, the greater their calorie intake, the higher the ratio of protein to methionine within the range tested, and the greater the percentage of fat in the diet, the more frequently were the lesions encountered in hearts and kidneys and the greater was the amount of fat in the liver.

Kesten *et al.* (1945) believed that at least 35% of ethyl laurate was necessary to produce death from cardiac necrosis. We have observed death in animals fed only 25% of the ethyl ester, although survival time was longer than the six days observed by the earlier investigators. Non-fatal degrees of cardiac necrosis have been observed when the amount of fat (lard) in the diet was only 2%, and even in fat-free diets.

The type of dietary fat employed was an important factor in the production of the lesion, aside from the factors mentioned above. Of the synthetic triglycerides employed, ethyl laurate produced the highest incidence of lesions when the animals' intake of food was adequate. The other triglycerides (C_6, C_8, C_{14}, and C_{16}) did not cause as extensive lesions as did ethyl laurate, and to this extent our findings are in agreement with those of Stetten's group. When the naturally occurring fats were used, beef fat and lard resulted in a considerably higher incidence of cardiac lesions than did corn or coconut oil. The reasons for these differences are not apparent at present.

Conclusions

1. Young male rats fed diets low in choline developed cardiac changes which were initiated by the deposition of stainable fat droplets in myocardial muscle, and which rapidly developed into widely distributed focal areas of frank necrosis. Liberation of fat droplets from necrotic muscle cells permitted their removal by tissue macrophages, so that the more advanced the necrosis the less prominent were the deposits of stainable fat. Choline chloride prevented the accumulation of significant deposits of fat and the development of cardiac necrosis.

2. The incidence of the lesions varied directly with the severity of the choline-deficient regimen, and therefore ran parallel to the degree of fat accumulation in the liver and the frequency of haemorrhagic renal lesions. Changes in heart muscle in 25 rats in which gross and microscopic changes did not develop in the kidneys suggested that the effect of choline-deficiency on the myocardium may be independent of its renal necrogenic action.

3. Cardiac damage developed in a few rats of a series fed a fat-free choline-deficient diet. The addition of high levels of fat to these diets greatly increased the number of animals with affected hearts. All types of dietary fat studied were not equally effective. Of the synthetic triglycerides tested, those of lauric acid (35%) in a choline-deficient diet produced the highest proportion of cardiac lesions, while tricaproin, tricaprylin, trimyristin, and tripalmitin were less effective. Of naturally occurring fats, beef fat and lard resulted in more cardiac damage in choline-deficient rats than did corn or coconut oil. The effectiveness of compounds of lauric acid in producing this type of cardiac damage confirms earlier observations of Kesten, Salcedo, and Stetten (1945), who first observed necrosis of heart muscle in rats fed choline-deficient diets containing 35–40% of the ethyl ester of lauric acid.

4. These findings, together with others concerning the accumulation of fat in coronary arteries of choline-deficient rats (Hartroft, Ridout, Sellers, and Best, 1952), and the frequent development of haemorrhagic renal lesions in similar animals, suggest that adequate supplies of lipotropic factors may be necessary for the maintenance not only of a healthy liver but also of normal cardiovascular and renal systems in rats.*

5. The authors propose that the definition of the term "lipotropic" be broadened to include the prevention of abnormal deposits of stainable fat in all organs of choline-deficient animals in which it has been demonstrated that this result is the direct outcome of lack of choline and its precursors.

These investigations were supported in part by grants from the National Research Council of Canada and from the Nutrition Foundation, Inc., U.S.A. Invaluable aid and advice were generously provided us by Professor C. C. Lucas and Dr. Jessie H. Ridout, both of the Banting and Best Department of Medical Research, University of Toronto, in the planning and preparation of the experimental diets. Mr. William D. Wilson, head histological technician in this department, was responsible for preparing many hundreds of frozen sections employed in this study. We are very much indebted to Dr. W. Lange, of Procter and Gamble, Inc., Canada, who generously provided most of the purified triglycerides. We would like to thank Professor Erich Baer, Banting and Best Department of Medical Research, for his most valuable help.

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*As this paper goes to press, Artom (*Fed. Proc.*, 1954, **13**, 176) has just reported that injection of choline into choline-deficient rats shortly before removal of tissues produced a greater rate of oxidation of fatty acids in slices of liver, kidney, and heart *in vitro* than in controls. Increases in production of radioactive $C^{14}O_2$ following administration of choline were observed in brain occasionally, never in testes. These findings lend support to the suggestion above, that choline deficiency may be the direct cause of the cardiac lesions described here.

A MORPHOLOGICAL SEX DIFFERENCE IN THE POLYMORPHONUCLEAR NEUTROPHIL LEUCOCYTES

BY

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AND

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[WITH SPECIAL PLATE]

Since 1949 Barr and his associates (Barr and Bertram, 1949; Barr *et al.*, 1950; Moore and Barr, 1953) have been demonstrating a morphological sex difference in the nuclei of the cells of the nervous system of mammals. In a recent paper (Moore, Graham, and Barr, 1953) they extended their observation to human skin and applied the method to the determination of the genetic sex in hermaphrodites.

For some time we have been considering the possibility of sex differences in the human blood, and at the same time we have been particularly interested in the nuclear morphology of the polymorphonuclear neutrophil leucocytes. Recently we have come to realize that there is a structural difference between the nuclei of the neutrophils in the two sexes, and we present evidence of this in the present paper.

Methods.—The routine blood films going through the department were used for the investigation. These were prepared on coverslips and stained on an automatic staining machine by the Jenner–Giemsa method. Only a very small number of films which were technically unsuitable were rejected. A few were stained by the Feulgen method. Many hundreds of films were examined in the preliminary studies. For the present investigation the neutrophils were examined in each of a series of 500 preparations.

Findings

While there is no doubt that chromatin condensations in the neutrophil nuclei are more striking in the female than in the male, this is very difficult to demonstrate in many films. It is easier to recognize the female by a solitary chromatin nodule, which becomes separated off from the main nuclear lobes in a proportion of the neutrophils (Plate, Fig. 1). This characteristic "drumstick," which is just visible at ×90 magnification, has to be distinguished from other appendages which occur in both sexes.

The drumstick has a well-defined, solid, round head, some 1.5 μ in diameter, joined by a single fine chromatin strand to one lobe of the nucleus. Undoubtedly some of these nodules are hidden or partly hidden by one of the lobes of the nucleus, but we have reckoned as characteristic only those which are discrete.

For the present investigation six neutrophils showing such discrete solitary nodules were sought in each of 125 female blood films. These were found on the average in 227 neutrophils; representing approximately 1 to 38 cells, the lowest being 1 to every 6 and the highest 1 to every 98 cells (Fig. A). The correctness of these average figures was confirmed in a further series of 250 female films, in which on the average the first cell showing the typical drumstick was the thirty-sixth counted (Fig. B). Several counts went above 98 cells.

Five hundred neutrophils were examined in each of 125 male blood films. In the majority nothing resembling a characteristic drumstick could be discovered. In an occasional preparation appendages were seen which might have been mistaken for the characteristic structure. Never were six of these discovered in 500 cells, and almost without exception they were rejected on closer scrutiny as minor lobes (Fig. 2), "small clubs" (Fig. 3), sessile nodules and tags (Fig. 4), and "racket" formations (Fig. 5). The minor lobes are too large, have two connecting strands, an irregular outline, or a deficiency of chromatin. The small clubs have a head less than 1 μ in diameter and are not visible at ×90 magnification; they are often multiple, and are perhaps more common in the male than in the female. Chromatin-rich sessile nodules and tags are more frequent in the female.

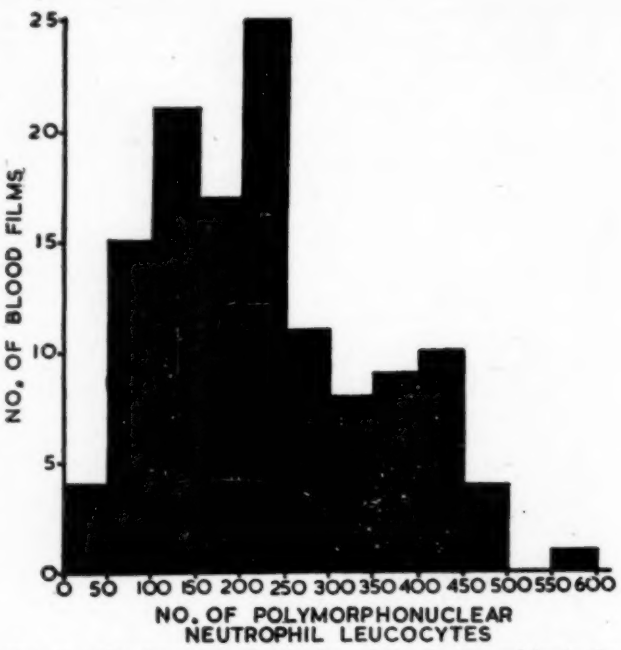

FIG. A.—The frequency distribution of the six drumsticks in the neutrophils in 125 female blood films.

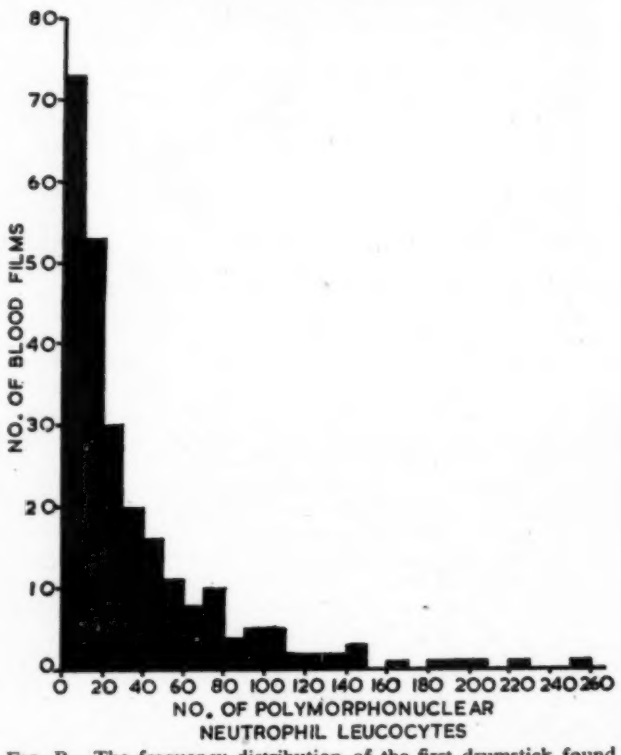

FIG. B.—The frequency distribution of the first drumstick found in the neutrophils in 250 female blood films.

The curious racket structures, which differ from the drumsticks only in having a pale centre, although rare, occur more frequently in the male.

The characteristic drumsticks are a feature of the lobulated nucleus of the mature neutrophil, are rarely found in the unsegmented forms, and have not been demonstrated in the precursory cells. They are therefore scarce where there is a shift to the left, particularly when it is of the toxic type, and they have not been demonstrated in the inherited shift to the left of the Pelger–Huët anomaly (Davidson *et al.*, 1954). Conversely, they tend to be more frequent where there is a shift to the right, but even in severe shifts do not appear in the male.

Age has no influence, drumsticks having been demonstrated from birth to 84 years.

Discussion

For many years entomologists have recognized the richness of the chromatin connected with the X chromosome, and have used this to demonstrate a difference between certain male and female cells, particularly when in mitosis (Geitler, 1937). Barr and his associates have extended these observations to the resting phase of mammalian tissue cells. We have found that a similar aggregation of chromatin can be demonstrated near the nuclear membrane of the polymorphonuclear neutrophil leucocytes, but with their irregular form it is difficult by this means to distinguish the female from the male. Taking advantage of the tendency of the neutrophils to form lobes and projections, we have found it easier to demonstrate a difference between the sexes when the female chromatin aggregation separates off as a drumstick-like projection.

It is tempting to think that the chromatin aggregation in the solitary drumstick represents the XX chromosome combination, as Barr and his associates have suggested for the cells of the nervous system and skin, and that the lesser aggregation of chromatin in the XY combination of the male either forms an insignificant projection or remains within one of the lobes of the neutrophil.

In over 50 of the films studied (over 25 from each sex) the sex was not known to the examiner. In no case was there an error in determining the sex. Only two proved difficult. They were both female films and undoubted drumsticks were found, but in one we had to count 585 cells before finding the sixth drumstick. In retrospect we realize that, in the main, the skew distribution of the drumstick counts is due to shifts to the left (Fig. A). This is undoubtedly a difficulty in a random sample of blood films, but we feel that a similar difficulty would arise with Barr's method with certain morbid changes in the skin. If films showing a marked shift to the left are excluded, six typical drumsticks should be found easily in the female within 500 neutrophils and none in the male.

This method of differentiating the sexes may be of medico-legal interest, and it has already proved of value to us in checking the origin of certain blood films.

Summary

A morphological difference between the polymorphonuclear neutrophil leucocytes in the male and those in the female is described.

A solitary nuclear appendage with a drumstick form is found only in the female.

Six such structures occur on the average in 227 neutrophils in the female and none in 500 neutrophils in the male.

The typical drumstick structures have to be distinguished from certain other appendages found in both sexes. These have been described.

We acknowledge our indebtedness to Professor H. A. Magnus for his interest and advice and to Mr. George Harwood, of his department, for the photomicrographs.

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THE TREATMENT OF INTERSTITIAL KERATITIS

BY

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[WITH SPECIAL PLATE]

Since the introduction of cortisone in hospital practice in this country, 20 cases of interstitial keratitis occurring as congenital syphilis have been treated at this hospital and closely observed for at least one year. Of these 20 cases, some had attacks of keratitis prior to the use of cortisone and suffered some visual impairment; in others keratitis was well advanced before such treatment. Eight of the 20 cases had had no previous attacks of keratitis or any visual impairment prior to the illness for which they were under treatment. It is these eight cases which are here reported.

Antisyphilitic treatment seems to have had little or no effect on the course and outcome of interstitial keratitis itself, but when congenital syphilis is first discovered by the appearance of this complication it is important that the patient and his family should be fully investigated and treated as necessary. Treatment with cortisone brings about rapid relief of symptoms and disappearance of signs of inflammation, and by the cutting short of the inflammatory period the likelihood of permanent scarring is greatly reduced. It is not certain that cortisone actually shortens the course of the disease. One must be prepared to continue with cortisone treatment for many weeks or months, and it may be necessary to restart treatment for the typical relapses and recurrences which arise.

Of the eight cases, three (Nos. 6, 7, and 8) had had full syphilitic treatment for at least a year, including not less than 8,000,000 units of penicillin before interstitial keratitis appeared. Case 6 had had attacks of keratitis several years previously and had had the usual treatment with mydriatics and systemic therapy. Of the other seven, who were in their first attacks, Cases 7 and 8 had been under routine general and local treatment for many months and interstitial keratitis was still obviously active before cortisone was given. The remaining five started cortisone and antisyphilitic treatment at the same time. All cases received at least 8,000,000 units of penicillin; most of them much more.

Treatment to the Eye

Cortisone.—In severe cases cortisone is given by subconjunctival injections of 10 mg. every third day, after the conjunctiva has been anaesthetized with 4% cocaine drops. This is continued until the eye is obviously settling. Relief usually appears in two to three days, and the third injection is not often required; subsequently, and for moderate cases, cortisone eye-drops (5 mg. per ml.) are instilled every hour by day. This is continued until the eye is white, when the frequency of instillation is reduced to one drop every four hours by day for two weeks, then three times

a day for another two weeks. Any sign of relapse is treated by returning to hourly drops.

Mydriatics.—Subconjunctival mydricaine, 5 minims (0.3 ml.), is injected daily until the pupil is widely dilated, then atropine drops 1% twice daily are used, returning to mydricaine as required. Mydriatics are discontinued as soon as the eye is white.

During the acute stage hot bathings and short-wave diathermy are comforting, and patients find relief from wearing dark glasses. Cases are kept in hospital in the acute stage; as soon as the condition can be controlled with local instillations they are treated as out-patients. This is usually after one week's treatment. If treatment can be started before the pupillary area of the cornea becomes vascularized, complete restoration of vision can be expected; corneal infiltration can be disregarded, as this will clear when the inflammation is under control. Clearing is slow, a completely "ground-glass" cornea taking six months to a year to achieve optical clarity.

Case 1

An unmarried woman aged 23 was seen on March 27, 1951, complaining of inflammation of both eyes of seven weeks' duration. For the previous 10 days she had received daily penicillin injections from her family doctor. At first attendance she was given 600,000 units of procaine penicillin and 1/5 gr. (13 mg.) of bismuth by injection. She was admitted to hospital the following day. In hospital the penicillin injections were repeated daily for 14 days. T.A.B. vaccine was given every third day in increasing doses of 25, 50, 75, and 150 million units. Guttae atropinae 1% were given twice daily to each eye. During this period the eyes became much worse and vision deteriorated. Cortisone therapy was considered.

On April 27 the general condition was as follows: left nerve deafness; blood W.R. +++, Kahn ++; tibial shafts showed a deposit of subperiosteal new bone consistent with old congenital syphilitic periostitis. The right eye showed conjunctival and ciliary injection; corneal epithelial oedema, deep infiltrates with rucking of Descemet's membrane; no vascularization. Keratitic precipitates and aqueous flare were present. Vision was reduced to counting fingers. The left eye was similar to the right, with central corneal disk-like infiltrates. Vision was reduced to seeing hand movement (Plate, Figs. 1 and 2).

It was decided to treat the left eye and use the right as a control. Atropine drops were instilled into each eye twice daily, with cortisone drops hourly to the left. In three days the left eye was white, and in six days the corneal opacity was noticeably smaller. By May 5, after eight days' treatment, the vision of the left eye had improved to 6/36. On May 18, after 21 days' treatment to the left eye, cortisone therapy to the right eye was begun with a subconjunctival injection of 10 mg. This was repeated after three days. After five days' treatment the eye was whitening and cortisone drops were given hourly. By June 18 both eyes were white and comfortable, and unaided vision was 6/12 right and 6/9 left. On June 24 all local treatment was stopped (Figs. 3 and 4). In August there was evidence of inflammation in the right eye with slight aching and redness. Cortisone drops, four-hourly, were begun, and all symptoms cleared within a week. Therapy was discontinued after three weeks, when vision was 6/6, right and left. Since then there has been no further sign of inflammation, and visual acuity has been maintained.

Case 2

This patient was a married woman aged 27. Congenital syphilis had been discovered at a routine antenatal examination two years previously. She had completed two years' antisyphilitic therapy before her eyes became affected. On February 12, 1952, she complained of pain and redness in both eyes just before her two previous monthly periods; these symptoms became worse, until the left eye was permanently red.

On examination there was conjunctival and ciliary injection of the left eye. By March 5 two small peripheral corneal infiltrates had appeared. Cortisone drops were given hourly by day to both eyes and atropine drops 1% daily to the left eye. After 10 days' treatment the eyes were white and comfortable, and the cortisone was then gradually reduced. No further symptoms have occurred, and vision in each eye has remained at 6/6.

Case 3

A man aged 36 first had acute right interstitial keratitis in June, 1951, with corneal infiltration and a salmon patch extending from 10 to 12 o'clock and on to the pupil margin. He was given routine systemic and local treatment as an in-patient for one week. The condition improved in three days and he was discharged from hospital after one week. The eye settled and there were no further symptoms until March, 1952, when he complained of dull aching pain in his right eye, aggravated by exposure to light. There was conjunctival and circumcorneal hyperaemia. Cortisone drops were restarted, with relief of symptoms. Cortisone therapy was tailed off and there were no further symptoms until July, when the right vision was 6/6. He then complained of slight pain in the left eye, which flushed to light. Cortisone drops four-hourly were prescribed for one week, when the eye was white; the drops were then gradually reduced. In July, 1953, the eyes were white and comfortable and vision was 6/6, right and left. There have been no further symptoms.

Case 4

A man aged 26 first attended in September, 1951, having been treated elsewhere for the previous year with systemic therapy and mydriatics. On examination both eyes showed circumcorneal hyperaemia with diffuse corneal opacities and no vascularization. He was treated with mydriatics, cortisone drops, and systemic antisyphilitic therapy. The eyes were white and comfortable, and the corneae were clear in one month. In May, 1952, the condition recurred: the right eye flushed to light and had central corneal infiltration with superficial vascularization above; the left eye showed central infiltration. Cortisone therapy was restarted for one month. In January, 1953, there was recurrence of inflammation, which again settled within two weeks with cortisone therapy. Since then the eyes have remained white and comfortable, and the vision is 6/6, right and left.

Case 5

An unmarried woman aged 22 was first seen in January, 1952, complaining of pain in the left eye for seven days. There was hyperaemia, with diffuse corneal infiltration, and a salmon patch was present in the upper temporal area. Routine systemic and local treatment was given, and she was discharged from hospital in 12 days. After two months the cornea was clearing. Mild symptoms persisted on and off until October, 1952, when the eye finally settled and all local treatment was discontinued. In October, 1953, the eyes were white and comfortable, and the vision was 6/6, right and left. There has been no evidence of further activity.

Case 6

A man aged 25 had interstitial keratitis in the left eye in 1946. This was treated for six months before it settled and finally cleared. He was admitted to hospital in December, 1951, with a history of pain in the right eye for three days. On examination the right eye was injected, with diffuse corneal infiltration and a salmon patch in the upper part. Treatment with cortisone drops hourly and atropine drops twice a day was begun. After three days the eye was whitening and more comfortable, and the salmon patch was reduced. The patient was discharged after 10 days in hospital. After 14 days the eye was white and the cornea was clearing. Atropine was stopped and cortisone drops were reduced. The condition recurred in March, 1952, with corneal haze and oedema reducing vision to 6/18. Cortisone therapy was repeated, and by April the eyes were

quiet, since when there has been no sign of activity in either eye. Vision in July, 1953, was 6/9, right and left.

Case 7

A girl aged 9 had been under treatment previously for congenital syphilis. On February 1, 1952, she was admitted with sore eyes. The right eye showed circumcorneal injection with some peripheral corneal infiltration and a deposit of cells on the posterior corneal surface. The left eye showed circumcorneal injection and superficial vascularization. Routine local treatment was begun with cortisone and atropine drops. In 48 hours the eyes were white and comfortable, and the patient was discharged on February 5, after four days in hospital, being then given treatment as an out-patient; this was gradually reduced, being discontinued on March 21. On two separate occasions the following year she developed circumcorneal hyperaemia, which was rapidly controlled by cortisone drops. Vision has remained at 6/9, right and left.

Case 8

A man aged 27 had been under treatment for congenital syphilis since May, 1947. On November 7, 1951, his left eye developed pain, redness, and photophobia. After treatment by his doctor, with no improvement, he attended hospital one month after the onset of symptoms. On examination the right eye showed circumcorneal injection only and vision was 6/6. The left eye showed conjunctival and circumcorneal injection with a diffuse corneal haze and a salmon patch in the upper part. Vision was reduced to counting fingers. Routine systemic and local therapy was begun. By November 19 the right eye was white and the left eye whitening. By November 26 both eyes were white and comfortable. Treatment was reduced, being discontinued on December 22. When last seen (July, 1953) both eyes were white and comfortable and the vision was 6/6, right and left. There have been no subsequent symptoms.

Conclusion

The use of cortisone in a series of cases has changed syphilitic interstitial keratitis from a long and painful illness, with the sequelae of defective vision or blindness, into an acute condition lasting only a few days. The condition is one which can easily be kept under control until the eyes are quiet and the vision is restored. Except for very acute cases, only out-patient attendances are required. If treatment can be started before corneal infiltration obscures vision, sight need not be impaired at any time.

I wish to express my gratitude to Dr. G. L. M. McElligott and Dr. F. J. G. Jeffriss, of the special clinic at St. Mary's Hospital, for their co-operation and assistance, and to Dr. P. N. Cardew, of the photographic department, St. Mary's Hospital, for the illustrations.

In his report for 1953, Dr. J. F. WARIN, M.O.H., Oxford, records a successful attempt to get closer co-operation between general practitioners and health visitors. Towards the end of the year, discussions were held with groups of medical practitioners, and it was agreed to allocate a health visitor to each doctor. The intention was that they should meet each other from time to time and so develop a closer working arrangement. Dr. Warin is able to report that great good will was shown on both sides and a much closer working relationship is already apparent. The vital statistics for the year show for the fourth consecutive year a very slight increase in the birth rate at Oxford, coupled with a slight decline in the high level of the illegitimate birth rate. Cancer of the lung remained a very frequent cause of death, though there were slightly fewer deaths in males than previously. Cancer of the stomach was three times as common in males as in women—an unusually high proportion.

PHONOCARDIOGRAPHY

BY

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[WITH SPECIAL PLATE]

Phonocardiography is the study of the graphic registration of heart sounds and murmurs. The heart sounds and murmurs were first recorded by a modified Frank capsule. This consists of a thin rubber membrane sealing the end of a tube leading from a stethoscope bell. A small mirror is attached to the margin of the membrane and the phonocardiogram is recorded by photographing a light beam reflected by this mirror. The apparatus is difficult to use, and as successive membranes differ in thickness the sensitivity to low-frequency vibrations is variable. Despite these difficulties an excellent monograph on the heart sounds and murmurs was published by Orías and Braun-Menendez (1939).

Recent advances in electronics have enabled much more satisfactory apparatus to be produced. In 1941 Rappaport and Sprague described the physical laws that govern auscultation and phonocardiography, and the Sanborn Company produced a phonocardiograph incorporating this knowledge. The sounds and murmurs are picked up by a crystal microphone and recorded on a multi-channel electrocardiograph by a special mirror galvanometer. This instrument is outstanding both because of the high quality of electronic workmanship and because of the proper understanding of the problem of "frequency response." The numerous commercial and privately built phonocardiographs which have not had an adequate frequency response have hindered rather than helped the advance of knowledge of the heart sounds and murmurs. It is for this reason that a brief description of the problem of frequency response is given.

Frequency Response of Phonocardiographs

The human hearing mechanism has a sensitivity which falls off in a logarithmic manner over the frequency range 1,000 to 20 cycles per second, and below this all vibrations are inaudible. Rappaport and Sprague insisted that the phonocardiogram would not resemble the auscultatory findings unless the instrument had exactly the same logarithmic response. A logarithmic tracing from the cardiac apex of a patient with mitral stenosis is shown in Fig 1 (Special Plate). If the instrument did not have a logarithmic response but recorded all the vibrations present in this area with an amplitude proportional to their actual intensity the frequency response would be "linear" (over the range 1,000 to 1 cycle per second). This linear phonocardiogram is in fact used as a reference tracing, and is called the "apex cardiogram." It does not show the heart sounds and murmurs because of the unattenuated low-frequency vibrations. The required detail will appear only when the tracing is enlarged twenty thousand times, and thus the logarithmic record is obtained only when the lower frequencies of the enlarged tracings are so reduced by filters that the high-frequency vibrations alone remain. Intermediate forms of frequency response may be of scientific value, but the tracings should not be compared with auscultatory findings.

The Heart Sounds and Murmurs

When there is uncertainty about the auscultatory finding the phonocardiogram is of great value. This occurs particularly when murmurs are minimal in intensity or

unusual in nature, or when tachycardia makes auscultation difficult. Particular examples of the value of phonocardiography in clinical medicine are best described under the individual sounds and murmurs. The normal phonocardiogram is illustrated in Fig. 2 for comparison with the later illustrations.

First Heart Sound.—When there is a loud systolic or diastolic murmur the first heart sound may not be distinguishable on auscultation, but the phonocardiograph will show that the vibrations of the first sound are slightly different from those of the murmur (Fig. 8). Occasionally the phonocardiograph shows that the first heart sound is absent and that a sound in early systole was mistaken on auscultation for the first sound. Sometimes a presystolic murmur is diagnosed on auscultation when the phonocardiogram shows a crescendic first heart sound. This mistake would not occur if the diagnosis of mitral stenosis were made only when a mid-diastolic murmur is heard. In mitral stenosis the first sound is delayed and the degree of delay as measured from the phonocardiogram may in future indicate the severity of the mitral stenosis.

Second Heart Sound.—The physiological splitting of the second heart sound due to asynchronous closure of the pulmonary and aortic valves is well shown on the phonocardiogram. The aortic component can be identified because it is better conducted to the apex. When the second component of the second sound is of low intensity it may be inaudible because of the fatiguing effect on the human hearing mechanism of the loud first component. The lack of fatiguing effect in the phonocardiograph reveals the extra sound. It is largely due to phonocardiography that the "opening snap" of the mitral valve is now diagnosed rather than "splitting of the second sound in mitral stenosis." The *claquement d'ouverture* had been described long ago by Potain, but has only recently been widely accepted. The phonocardiograph shows a series of high-frequency vibrations at the onset of the "R.I." wave of the apex cardiogram (Fig. 1) and often shows this sound when it is inaudible on auscultation (Fig. 7), which is valuable evidence of the presence of mitral stenosis.

Third Heart Sound.—It is difficult to differentiate on auscultation between a long third heart sound and a short diastolic murmur. The phonocardiogram enables the duration of the vibrations to be measured, and should they last more than 0.16 second they constitute a diastolic murmur. Over the age of 30 a third sound is of serious significance unless it occurs only with tachycardia, when it may be due to "summation gallop." When the nature of gallop rhythm is uncertain the phonocardiograph will clarify the problem.

Systolic Murmurs.—The phonocardiogram is very useful in distinguishing the ejection murmurs of pulmonary and aortic stenosis from the murmurs of mitral or tricuspid regurgitation or ventricular septal defect. The ejection murmurs are diamond-shaped and that of aortic stenosis ends before the second heart sound (Fig. 5). The murmur of pulmonary stenosis reaches the aortic component of the second sound but ends before the delayed pulmonary component (Fig. 6). The murmurs of mitral and tricuspid regurgitation and ventricular septal defect fill the whole of systole (Figs. 7 and 8). The tricuspid murmurs are of more variable intensity than the others, and often show a marked change during respiration.

Diastolic Murmurs.—When the murmur of aortic or pulmonary regurgitation is audible at the apex it may be difficult to decide whether there is also a mitral diastolic murmur or an Austin Flint murmur. The phonocardiogram of the aortic or pulmonary diastolic murmurs has a characteristic crescendo and decrescendo pattern (Fig. 10). This can be distinguished from the pattern of the diastolic murmur of mitral stenosis, which does not start until after the opening of the A–V valves and is composed of coarser and more irregular vibrations (Fig. 9). The late first sound and "opening snap" of the mitral valve also confirms that mitral stenosis is present.

Continuous Murmurs.—The phonocardiogram of the murmur of persistent ductus arteriosus shows that the intensity of the vibrations is maximal at the time of the second heart sound and minimal at the beginning of ventricular systole (Fig. 11). When the to-and-fro murmurs of pulmonary or aortic valve disease coexist the phonocardiogram often helps to identify the separate murmurs. Other continuous murmurs due to such conditions as arteriovenous aneurysms or rupture of a sinus of Valsalva into the right ventricle may show features which are most easily identified by the phonocardiogram (Fig. 12).

The Future of Phonocardiography

The phonocardiograph has helped to build our present knowledge of the heart sounds and murmurs and will continue to add to this knowledge. In this respect it is like the electrocardiograph, which has taught us much of what we know about the heart and yet is of relatively little value now that this knowledge has been obtained. The use of phonocardiography is certain to increase in several ways. It will be used more and more for teaching, especially in conjunction with the tape recorder. The phonocardiogram during Müller and Valsalva manœuvres and in other physiological experiments will gradually replace the tracings taken at rest as a means of identifying unusual murmurs. Finally, the phonocardiogram itself will be used more and more as a reference tracing in order to time other graphic investigations of cardiac activity.

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MISSILE WOUNDS IN MALAYA

BY

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This report covers the three-year period from January 1, 1950, to December 31, 1952. The "emergency" in Malaya began in July, 1948, and from then until the end of 1949 there were 197 missile casualties sustained on operations and treated in military hospitals, with 14 deaths from wounds, including deaths before arrival at hospital. Unfortunately, records permitting detailed analysis of missile wounds during this period are not available in FARELF. On assuming responsibility for surgery in the Far East Land Forces in July, 1950, I introduced a system of reporting all missile wounds in synoptic form, which has enable an analysis to be made of wounds received from the beginning of 1950, the treatment given, and the progress made. The scale and tempo of the campaign in Malaya made this possible. Also the circumstances were probably unique in modern military surgery; for casualties were admitted direct to military hospitals, where they were treated by the same surgeon until convalescent or repatriated. This has been of the greatest value.

I spent the first half of 1950 as surgeon at the military hospital at Kuala Lumpur, where casualties were admitted direct from the jungle. Subsequently I saw most of the seriously wounded cases, either during routine visits to hospitals or when they were evacuated to Singapore, where such cases normally come under my personal care.

Nature of the Malayan Operations

The anti-terrorist operations in the Federation of Malaya have followed the usual pattern of this type

of warfare, but have been made especially difficult by the densely wooded nature of the terrain. There is nothing of the nature of a front. The enemy, merging at will with the general population, who feed them, strike irregularly at widely scattered points which cannot be anticipated. Ambushes of patrols sent out to investigate an "incident" on a rubber estate, ambushes of vehicles on roads and tracks, firing at railway coaches from the jungle—these are the typical methods of attack, and, with conditions so suited for surprise, the only really remarkable feature of the Malayan operations has been the surprisingly low number of casualties inflicted on our troops. Added to those from enemy action are the inevitable accidental wounds which occur when a large number of men of varying intelligence are constantly in possession of highly lethal weapons, usually loaded.

The surgical problem has been to manage, with limited resources, missile wounds and other injuries occurring unexpectedly at widely separated points over the whole of Malaya, often singly and never in large numbers (incidents in which there were more than 12 casualties were exceptional). Some occurred far out in the jungle, others close to a hospital, others again on a train in the middle of the night. As a result the time taken for a wounded man to reach a hospital, where he first received adequate surgical treatment, has varied from less than an hour to 96 hours. The average delay between wounding and surgical operation has been between 10 and 12 hours.

Surgical Dispositions

With no possibility of providing close surgical support for widely scattered forces, the surgical plan has been to provide centres at strategically placed military hospitals, to which casualties were brought by whatever means were available—road, rail, air, or river. These hospitals are at Taiping, covering North Malaya, at Kuala Lumpur, covering Central Malaya, and at Kluang, covering South Malaya. Casualties from South Johore went direct to Singapore. Limited emergency facilities were also provided in Pahang, where a field surgical team was located, and at the Cameron Highlands.

Use has also been made of the civil hospitals in Malaya, and we have been greatly indebted to the Malayan Medical Service for ready co-operation and assistance. Most towns of any size have a hospital, but in only a few large towns are full surgical facilities available, and, whenever possible, casualties were transferred to military hospitals either direct or after emergency treatment. The main surgical cover was at Singapore, where, at the large modern well-equipped military hospital, specialized facilities existed for orthopaedics, maxillo-facial surgery, otolaryngology, and ophthalmology. Cases beyond the scope of the up-country hospitals were transferred there. These included neuro-surgical and thoracic cases and all long-term cases.

Use of Helicopters

With casualties occurring at widely separated points, often deep in the jungle, quick evacuation to hospitals has proved a major problem, still not satisfactorily solved. Until a road or suitable river was reached, casualties usually had to be hand-carried, the entire patrol taking turns and providing protection. At the roadhead, rendezvous with an ambulance was made and the casualties were taken to the nearest medical installation, which may or may not have been a surgical centre. In the latter event they were transferred after first aid and resuscitation, but the necessity of avoiding undue delay over this was stressed. A casualty evacuation flight of four HC 2 (Dragonfly) helicopters has been available for lifting wounded since the end of 1950. From the surgeon's viewpoint this is almost the ideal method, and few things are more spectacular than a successful helicopter evacuation, the casualty, after preliminary first aid, being transported rapidly and landing on the football ground adjacent to a military hospital. However, despite numerous successful helicopter evacuations, this method has not yet proved to be the final answer to jungle warfare, and the majority of cases must still be hand-carried to roads, where they can be met by jeep or ordinary motor ambulance. The reasons for this are various.

Difficulties in maintenance of these expensive and complicated aircraft, which were based on Singapore Island, made it impracticable for them to be located strategically throughout Malaya; in fact, it often proved difficult to keep more than two aircraft fully operational at any one time. This meant delay in getting them from Singapore. Also, the helicopter must have a cleared area in which it can land safely. Because of reflected air currents it is dangerous to attempt landing close to tall trees. Although experiments have been made in "winching" patients direct to a hovering helicopter, the difficulties and risks of such a manœuvre in the jungle exclude this at present from the field of practical evacuation save in exceptional circumstances. This means that a casualty must be carried to a suitable cleared area if one exists in the locality. The preliminary selection of suitable sites for this is important if not always practicable. Should the helicopter pilot, normally guided in by Auster aircraft, regard the site as unsuitable, much time, possibly an entire day, would be wasted and the casualty would have to be taken back by traditional methods. The limitations of helicopter evacuation in dense jungle country can thus be appreciated.

On the other hand, movement by air between main towns up and down the Malay Peninsula is rapid and easy except at night, when the absence of night-landing facilities on some airfields prevents it. It has therefore been practicable to send certain types of case—for example, head wounds, spinal injuries, maxillo-facial wounds, etc.—direct to Singapore for specialized treatment not available up-country. A regular air ambulance service (Valetta) up and down the peninsula has been maintained by the R.A.F. once a week for the routine transfer of cases.

Resuscitation and Transfusion

With the relatively long time-interval between wounding and surgical treatment, the prevention of blood loss has more than ever been a matter of the utmost importance. Second only to this have been the speedy replacement of blood already lost and the prevention of infection. The last of these has proved much the easiest to achieve. As the amount of blood replacement required is determined by the amount lost, the major effort has been directed to minimizing blood loss by effective immediate first aid. A vigorous drive on first-aid training for all ranks with an operational role has paid handsome dividends. Most of the wounded when first seen by surgeons were reported to be in good general condition, with first-aid dressings adequately applied and fractured limbs efficiently splinted. The odd exceptions to this have merely emphasized the overall good standard and, when possible, have been made the excuse for a renewed drive on first-aid training. Initial first aid has been made primarily the responsibility, not of medical orderlies, who are seldom immediately available, but of the man's companions; and his immediate commander, irrespective of rank, is held responsible for seeing that this is done. With constant personnel changes in units, first-aid training must be frequently repeated—in fact, it should be almost continuous, a point which is apt to be forgotten. In controlling haemorrhage the emphasis has been on direct pressure correctly applied.

Blood Replacement.—Whole blood has been preferred. Initially, Group O blood was used after direct cross-typing. This was later changed to the correct group when this had been determined, if continued transfusion was necessary.

Experience has shown that, in general, the more blood a casualty receives the better he does. This has been found to be of particular importance in determining whether or not a wound will heal by first intention after suture, in limiting or preventing minor wound infection, in accelerating bone union and skin cover, and in shortening convalescence generally. In fact, in nearly all cases in which healing has been delayed, a check on the blood has revealed a lowered haemoglobin content and blood protein. Most wounds of any severity require four to five pints (2.3 to 2.8 litres) of blood, or more if bleeding has been considerable. In addition a watch on blood haemoglobin and blood protein is necessary during the two weeks following operation in all severe cases, and any fall, which is usual, should be corrected by further transfusion. The difference between cases so treated and other cases has been remarkable.

Plasma.—Plasma was occasionally used as a preliminary to whole blood while the latter was being cross-matched and prepared. An interesting observation has been made about the storage of plasma in the Tropics. It was found at one stage that plasma (1945 and 1946 vintage) was causing a high incidence of reactions, mainly rigors and sometimes severe. In one hospital the incidence was 30%. Investigations showed that the plasma had been stored for a considerable time (six months or more) at room temperature, which in Malaya is about 80° F. (26.7° C.). The plasma came to Malaya as refrigerated cargo and was kept refrigerated until issued to hospitals. When plasma which had been in continuous refrigeration was used the incidence of reactions abruptly ceased. Despite the common view that plasma can be stored at room temperature almost indefinitely, the experience in FARELF has suggested that some slow biochemical change does in fact occur in stored plasma, and that this is greatly accelerated by storage in a tropical temperature.

Plasma Substitutes.—Apart from a short trial with dextran these have been little used. The need for them has not so far arisen.

Antibiotics and Chemotherapy

In order to provide uniformity of treatment and to minimize the development of resistant strains, the following courses and dosages were adopted throughout the command :

Forward Treatment.—After securing haemostasis the wound was lightly dusted with a sulphonamide-penicillin powder, avoiding excess. This was done when possible, but was not regarded as essential. After appropriate dressing, splinting, etc., 200,000 units of penicillin was given intramuscularly. Procaine penicillin has now largely replaced crystalline for this purpose in forward areas. Injections of 200,000 units were repeated twelve-hourly (procaine) or six-hourly (crystalline) until hospital was reached. Prophylactic oral sulphonamides were considered unnecessary, as carrying a risk of sulphonamide anuria in this climate.

Hospital Treatment.—For ordinary wounds penicillin was continued in the same dosage, 200,000 units six-hourly or twelve-hourly, according to the type used, for five to seven days. For more serious wounds (extensive soft tissue, bone and joint, penetrating abdominal, severe multiple, etc.) or where there was evidence of established infection, a loading dose of 500,000 units of penicillin was given on admission, followed by 200,000 units twelve-hourly (procaine) or six-hourly (crystalline) for seven to ten days.

Penicillin in excess of the above dosage was rarely found necessary, though surgeons used their discretion. Supplementary sulphonamide therapy also was left to the discretion of the surgeons, but as a rule was used only when there was established infection. Sulphadimidine was preferred, and a full course was insisted upon. Streptomycin was normally given only in cases with penetrating abdominal wounds. The other antibiotics, though available, were little used. The policy was to try to prevent the development of resistant strains by keeping to penicillin in large doses and holding the other substances in reserve. This was so successful that wound infection was exceptional and resistant strains were almost unknown.

Clostridial infection was seen in only three cases—two of clostridial myositis and one of clostridial cellulitis. All cases recovered. No case of tetanus occurred.

It would appear from Malayan experience that under favourable circumstances wound infection could become almost entirely eliminated. Four factors of almost equal importance are necessary to achieve this : (*a*) Adequate antibiotic therapy started as soon as possible after wounding and continued for approximately one week after wound toilet. (*b*) Adequate wound toilet ; it is essential that no debris or devitalized tissue be left. (*c*) Adequate blood replacement, repeated as necessary during post-operative convalescence. The aim should be to maintain blood protein and blood haemoglobin at a level as close to normal as possible. If this is done wounds will normally heal by first intention or be ready for skin cover within a few days. This requires more blood than is customarily given. (*d*) Complete rest of the wounded part for the next 10 days.

The first two conditions are easy to achieve. The third requires careful organization, and may be difficult if casualties occur unexpectedly in large numbers. Here plasma is a useful temporary substitute for whole blood. The fourth is normally impossible in war, but its importance wherever local conditions make it temporarily practicable (as in Malaya) is well illustrated by comparing our results with those in Korea. During a visit to Korea and Japan early in 1952 I noticed that a considerable number of casualties with wounds involving bone had developed wound infection by the time they reached hospitals in Japan from Korea, in spite of full antibiotic therapy, adequate wound toilet, and liberal blood replacement. This was in contrast to our own experience, in which established infection had been exceptional. The only difference was that their cases usually had to be moved from Korea to Japan during the first post-operative week, whereas ours remained in hospital, ensuring complete rest and enabling rather earlier delayed primary suture and, in selected cases, even primary suture to be performed. There seems to be a critical stage in the first few days after wound toilet, particularly if bone is involved, when any form of movement, however slight, may be sufficient to enable penicillin-resistant organisms to establish themselves. Any lowering of blood protein or haemoglobin also favours this.

Casualty Figures for 1950–2

The figures in Table I refer to missile wounds only, whether from enemy action or accidental, the latter including any self-inflicted wounds. They include all cases treated in military hospitals during the three-year period ; and, except for a few police and civilian casualties, which were later transferred to civil hospitals, all were Service personnel.

TABLE I.—*Casualty Figures*

	1950	1951	1952	Total
Wounded admitted to hospital ..	203	317	254	774
Died in hospital	13	19	11	43

Of the 774 casualties reaching hospital alive, 14 died soon after admission without any surgery except attempted resuscitation, and one death occurred in a civil hospital. The remainder were operated on and 28 died, giving an operative mortality of 3.7%. The overall mortality was 5.5%. The policy was to give every possible case the chance of surgery.

Enemy action accounted for 62.5% of the casualties admitted. The relatively high proportion of accidental wounds was mainly because battle casualties were remarkably few.

As might be expected from the type of warfare—that is, short-range ambush—the proportion of killed to wounded was high. In a series of 592 casualties from enemy action during the period under review and occurring among

military personnel about whom full details are available, the mortality figures were:

Total casualties in series ..	592
Reported "killed in action" ..	171 (28.9%)
Reported "died of wounds"	32 (5.4% of total casualties; 7.6% of wounded)

Of the latter, 15 (2.5% of total casualties, 3.6% of wounded) died in hospital, the remainder en route. Thus although the mortality among casualties from enemy action was over one in three, four-fifths of these were killed in action.

Despite the relatively long delay before surgery, the overall shortage of experienced surgeons, and frequent changes due to the relatively short stay of National Service officers, the results have progressively improved with accumulated experience of local conditions (Table II).

The operative mortality in Burma in 1945 was 7.6%.

TABLE II.—*Operative Mortality*

Period	Cases	Total Mortality	Operative Mortality
1950	203	6·4%	5·4%
1951	317	6·0%	4·1%
1952	254	4·3%	1·6%

Cause of Death

The fatal cases may be grouped as follows:

Resuscitation only, no operation	14
Died during operation	3
Failed to recover from shock	15
Septic complications	3
Post-shock renal failure	4
Other causes	4

These figures indicate where better results might have been possible. With one exception, those who were regarded as unfit for surgery died soon after admission, and their cases appear to have been hopeless. The exception was an abdominal casualty who failed to respond to resuscitation and died 10 hours later. Early operation might have saved him. The three septic complications were cerebral abscess, suppurative pericarditis, and lower-limb gangrene in which amputation had been unduly delayed. The four "other causes" were air embolism, cardiac tamponade, bronchopneumonia after craniotomy, and perforation of a thoracic stomach. All the others died directly or indirectly from the results of haemorrhage. The three deaths under anaesthesia occurred in attempts to arrest uncontrolled bleeding in chest wounds. Fifteen failed to recover from their post-operative shock, some dying soon after operation, others surviving as long as the second post-operative day. Four survived operation only to die of renal failure on the third, fifth, twelfth and twentieth day. In an endeavour to improve results, efforts were mainly directed on the group failing to recover from shock. More rapid evacuation, more individual experience in war surgery, and more liberal blood replacement may well have improved these results. Greater use of helicopters seems to be the only method of speeding evacuation.

The two factors in the present series which most influenced the mortality figures of those surviving to reach hospital were the experience of the surgeon available and the facilities for resuscitation and post-operative management. Whenever possible all serious cases should be evacuated direct to centres with full facilities, even though this may take longer. Here the helicopter is invaluable, because, once the case is airborne, distance within reason has little meaning and the extra time involved is well spent. Malayan experience has been that, provided first aid is good and resuscitation sufficient to maintain the blood pressure, time is no longer the overriding consideration, thanks to the antibiotic drugs.

Wound Toilet and General Operative Technique

Standard methods have been employed, following the experience gained during the second world war, and their use has served only to confirm their soundness. The excellence of present-day anaesthesia means that, once haemorrhage has been arrested, and with blood pressure under control and a blood drip running, time is not such a vital factor as to preclude adequate wound toilet. If this is thorough and blood replacement is adequate, complications from infection can be almost entirely eliminated, provided the patient does not have to be moved during the post-operative phase.

The only departure from standard teaching has been a return to primary suture in selected cases. This has been done because of the special circumstances of war surgery in Malaya. The avoidance of primary wound closure was one of the clearest surgical lessons of the second world war. It was therefore not without some thought that this practice was modified. However, the conditions which demanded delayed primary suture in the Western Desert and elsewhere did not apply in Malaya. Wound contamination has been minimal in the jungle: casualties go direct to military hospitals, whence there is normally no necessity to move them again until they are convalescent. Penicillin is available in large doses, and casualties never arrive in such numbers that immediate surgery is not available.

Under these conditions, and with the types of wound received in this theatre of operations, it was felt that, in selected cases, primary suture was not merely justified but might actually become the method of choice, especially when bones and joints were involved. In consequence, primary suture has been recommended, for example, in penetrating wounds of the head and chest and in wounds of the face, hand, and joints; and has been permitted at the discretion of surgeons in other suitable wounds. Necessary conditions were that there was no evidence of infection, wound toilet was adequate, and the case could be retained under the personal supervision of the surgeon for the next two weeks. In no case in which these conditions were complied with was wound infection seen. A few cases, sutured and transferred, mostly from small civil hospitals, after apparently inadequate toilet, arrived infected, and served to illustrate the danger of this method if applied to cases to be transferred. The figures are: treated by delayed primary suture, 434 (51.3%); treated by primary suture, 305 (36%); treated conservatively, 107 (12.6%).

Wounds treated conservatively had skin excision only, and were practically confined to certain clean through-and-through wounds of the chest, shoulder, and feet, or to multiple minute peppering.

It must not be taken (because of the use of primary suture in selected cases in Malaya) that there has been any change in the official teaching that, normally, primary suture has no place in military surgery. Delayed primary suture must remain the standard method of treating war wounds, except where exceptional circumstances may make deviation from this policy possible. To attempt otherwise is to court disaster.

Penetrating Wounds of the Head and Spine

The number of cases with penetrating wounds of the head and spine admitted was remarkably low despite the fact that steel helmets are not worn in Malaya. This is perhaps because most head wounds, which were nearly all inflicted at short ranges, killed outright or the casualty failed to reach hospital alive. For example, of nine men with head wounds among British troops during 1952, five were brought in dead. Only 3 cases of spinal and 15 of head wounds were admitted during the three-year period. Of the latter cases, seven were from enemy action, three were suicides, and five were accidental. Five patients were moribund on admission and died soon after; the remaining 10 had craniotomy performed, with 4 deaths. Operations were by general surgeons. Of the three patients with spinal wounds, one with quadriplegia died the same day, while two paraplegics survived to be repatriated. The average delay before operation for head wounds was 12 hours.

Penetrating Chest Wounds

There were 57 penetrating chest wounds (excluding thoraco-abdominal) in the series, with 10 deaths. The average delay between wounding and surgery was eight hours. All cases not moribund on admission had wound toilet and closure of the chest defect with primary suture wherever possible. Subsequent management depended on the special indications and is shown in Table III.

TABLE III.—*Penetrating Chest Wounds*

Treatment	Cases	Deaths
Resuscitation only	2	2
Wound toilet only	21	7
Wound toilet, thoracentesis as required	20	—
Wound toilet, thoracotomy, thoracentesis as required	13	1

These chest wounds have been among the most difficult on which to make a decision. Standard teaching, based on war experience, is that conservative treatment by wound closure, blood replacement, and repeated aspiration is the method of choice, reserving thoracotomy for cases with definite indications, and I think most experienced surgeons are in agreement with this. Nevertheless, in this series conservative treatment had a mortality rate three times that of thoracotomy. Let us examine the causes of death.

The only death after thoracotomy occurred rapidly from cardiac tamponade, 60 hours after operation. A piece of mortar shrapnel had been removed from the right pleural cavity and another piece had been felt deeply behind the heart and left as inaccessible. Of the other deaths, one followed perforation of an unsuspected intrathoracic stomach in an apparently simple through-and-through wound; two occurred soon after admission, with no surgery apart from attempted resuscitation; two occurred under anaesthesia (one during induction), both with uncontrolled bleeding; and the remainder were caused by shock within 48 hours of simple wound toilet and closure. Thoracotomy may have saved some of these, though three had severe wounds elsewhere.

In general the tendency has been for surgeons to explore the chest more often as their experience increased, the main indication being a fairly large retained fragment or evidence of severe or continued bleeding. In most cases lung lacerations were found, requiring closure, two being so extensive as to need lobectomy. There are two fallacies about chest wounds which are still apparently taught and which require exploding. One is that it is dangerous to give blood to chest cases, the other that it is equally dangerous to give morphine. Chest wounds with blood loss need adequate blood replacement just as urgently as wounds elsewhere, and, provided it is given intelligently, not too quickly, and as whole blood, this appears to carry no more risk of acute pulmonary oedema than transfusion therapy generally. Similarly, chest wounds require morphine or a similar drug in dosage sufficient to permit breathing without pain and even coughing without undue distress. It is the inability to breathe comfortably or to cough which is the main cause of failure of lung expansion and not depression of the respiratory centre by morphine, which is largely theoretical with the dosage required. When a patient's condition is precarious the ability to breathe comfortably is of great importance, and his failure to do this because of pain may well tilt the scales fatally against him.

Ultimate lung re-expansion was obtained in all cases, and usually this was rapid once surgeons appreciated the common cause of early non-expansion—that is, a plug of mucus in a bronchus. The pleural effusion on which attention tends to be focused is usually secondary to this. Only one case required decortication of the lung. Here infection of the effusion had occurred. Except for those British soldiers who were repatriated as part of the general policy, all chest cases ultimately returned to duty.

Abdominal and Thoraco-abdominal Wounds

There were 60 cases in this group, and all except 4 were operated on. The results are shown in Table IV.

TABLE IV.—*Abdominal and Thoraco-abdominal Wounds*

		Cases	Deaths	% Mortality
Abdominal	Not operated on	2	2	100
	Operated on	36	6	16·7
Thoraco-abdominal	Not operated on	2	2	100
	Operated on	20	5	25

More surgical experience and more liberal blood replacement might well have reduced the mortality. Over half the total cases were operated on by junior surgeons with no previous experience in war surgery and only a limited experience in abdominal surgery. My personal experience has been that, provided blood replacement is liberal and surgery adequate, most abdominal wounds do well if operated on in reasonable time. So much so, that when these cases go wrong it rather suggests that there has been some error in technique or that the patient has been allowed to drift into an irreversible state of shock.

All abdominal cases were treated post-operatively with gastric suction and intravenous drip until bowel activity was well established. Of the 20 thoraco-abdominal cases operated on, 7 were approached via the chest, 12 via the abdomen, and one by both routes.

The average delay between wounding and surgery was 8.5 hours in 41 cases in which this information is available.

Bone and Joint Wounds

There were 223 patients in this group, with 9 deaths. Three of these had other severe associated wounds (two with penetrating abdominal wounds) which were the cause of death, and two were admitted moribund. Of the remaining four, two died of renal failure, one died from oligaemic shock with inadequate blood replacement, the degree of blood loss not having been appreciated, while the fourth died from fat embolism 24 hours after a wound of the upper tibia.

Excluding those dying from associated wounds, the mortality in the group was 2.7%. Many of the hand and foot wounds were self-inflicted and involved metacarpals, metatarsals, or phalanges, and in addition there were a number of soft-tissue through-and-through wounds of the hands and feet which have not been included. Shooting oneself through the hand or foot was the commonest accident with weapons, and the majority seem to have been genuinely accidental. Morale was high in Malaya, with little evidence of deliberate self-infliction.

There were no special features about bone and joint wounds, which were treated by standard methods. The principles aimed at were thorough wound toilet, adequate blood replacement, adequate splinting with elevation where possible, and avoidance of movement. We were fortunate that circumstances in Malaya permitted this last principle to be followed in nearly every case, and the low incidence of infection seen was perhaps largely due to this, partly by permitting early suture but mainly by avoiding additional trauma during the next ten days or so, when bone and joint wounds seem to be peculiarly susceptible to invasion by penicillin-resistant organisms. It was found that adequately splinted wounds rarely became infected, whereas inadequately splinted wounds often did. Fortunately most of the few cases of established infection responded readily to the newer antibiotics. Experience showed that delayed primary suture is best done as soon as possible—that is, on the third or fourth day. If infection is going to occur it should be evident by then; if not, it is safe to close the wound, and the sooner exposed bone is covered the better.

If suture was delayed unduly secondary infection with penicillin-resistant organisms occurred; it was the experience with these cases which prompted the return to primary suture for selected cases. Results have justified this, and in the majority of wounds involving bone and joint uneventful first-intention healing was obtained and subsequent management was the same as that of a closed fracture.

Plaster-of-Paris was used for splinting in most cases. For upper-arm and shoulder-girdle wounds a well-padded spica was preferred. For wounds involving the knee-joint, or below, the Tobruk splint has probably proved the most effective method of immobilization: the all-important elevation can easily be obtained by this comfortable method. It is also suitable for lower-limb soft-tissue wounds, which do best when splinted in elevation. Similarly, the importance of keeping forearm and hand wounds immobilized in elevation has been repeatedly demonstrated. Provided this is done from the beginning, oedema of the hand and consequent finger stiffness are minimal. Early finger movements were insisted on.

When skin loss was extensive early skin cover was sought. Usually this could be combined with partial delayed primary suture and, when blood replacement was sufficient to keep the blood proteins up, a relatively high percentage take was achieved.

It is not possible accurately to assess final results with bone and joint wounds in Malaya because of the policy by which most severe cases in British troops were repatriated as unlikely to be fit for active operation within three months, and their ultimate disposal is unknown. However, of 128 British troops in this group 46 returned to duty, and of 48 Gurkha and African troops who were treated to finality nearly all had returned to duty; a few were still under treatment.

The average time between wounding and surgery in the bone and joint group was 12.5 hours in the 143 cases in which this information is available. The two longest delays were both 96 hours; in these two cases, a knee and a forearm wound, regular penicillin injection was not possible, and they were infected on admission. The only other cases reported infected on admission were a few which had been treated for some days elsewhere before transfer to military hospitals. With these exceptions wounds were clinically without evidence of infection on admission. Nevertheless primary suture was normally performed only on recent cases, those of eight hours or over usually having delayed primary suture, and the great majority healed by first or second intention without infection of the underlying bone. When this occurred it was typically in wounds in which skin cover had been difficult to achieve or had been delayed, or else, because of a fall in blood protein which had not been corrected, the wound broke down secondarily. These cases, after skin cover was obtained and any small sequestra were removed, practically all healed with suitable antibotic treatment. Very few still had low-grade infection when repatriated. No case required amputation because of chronic infection. Major amputation had to be resorted to in five cases only, all because of major-vessel injury and a non-viable limb.

These results are significant. They show that with the use of penicillin in adequate dosage wound infection can be long deferred and time as such ceases to be all-important. It is haemorrhage and shock which are most likely to kill these patients, and sufficient time should be taken to ensure adequate splinting and blood replacement. Good first aid is of the greatest importance.

Maxillo-facial Wounds

A senior dental specialist working with a senior surgeon was located at the Singapore Military Hospital, to which all maxillo-facial cases were transferred, usually by air and usually after preliminary toilet up-country.

In the 18 cases in this group the mandible was involved in 11, the maxilla in 7, and other bones in 2. Two men died from severe multiple associated wounds. Six British cases were repatriated; the others were treated to finality and returned to duty with satisfactory functional and cosmetic results. Treatment was on standard lines. The average delay between wounding and first surgical operation was 17.2 hours.

Soft-tissue Wounds

Of the 555 soft-tissue wounds reported, approximately two-thirds were major wounds. Each distinct major wound has been counted, but with minor wounds each casualty has been counted as one wound only, because the majority (over 80%) had received multiple grenade or buckshot wounds, involving soft-tissue penetration of many small fragments, to varying depth. Some of these required considerable surgical toilet, others were treated entirely conservatively. In general, small fragments were left. Minor wounds that were associated with major wounds have not been counted. Major soft-tissue wounds have been arbitrarily defined as those causing considerable muscle or other soft-tissue damage and demanding major wound toilet, also through-and-through wounds. Most of the major wounds in the group were treated by excision and delayed primary suture, which is still regarded as the only safe method where there is any degree of muscle damage.

In some sites, particularly the shoulder, small clean through-and-through wounds, such as those resulting from carbine bullets, were sometimes treated conservatively—that is, by skin excision only. No case of wound infection occurred after this, and recovery of function was usually much more rapid and complete than after extensive full excision. The skin wounds were left open for drainage. Most of these wounds occurred through a thin cotton shirt only. Shoulder wounds should be treated in abduction: some cases in which this was omitted had considerable shoulder-stiffness with limited abduction. Although this method is potentially dangerous and cases need careful watching, it was felt that, with the favourable circumstances in Malaya, the advantages outweighed the disadvantages for many shoulder wounds, and most cases returned early to duty with a full range of shoulder movements. For through-and-through wounds elsewhere, opening up and excision of the tract was the method normally adopted: conservative treatment is specially dangerous with through-and-through leg wounds.

Clean superficial wounds were usually excised and sewn up as in civil practice, generally with first-intention healing. Nevertheless, experience with primary suture in this theatre has done nothing to alter the standard teaching that it has little place in military surgery except where special local conditions approximating to ordinary civilian practice occur.

Soft-tissue wounds included 42 major nerve injuries. All British casualties were repatriated for treatment as long-term cases. Asian cases were treated locally.

Very few major vascular injuries occurred. Only eight major arterial wounds were recorded, of which five required amputation (upper limb one, lower limb four). One patient died in a civil hospital.

General Remarks

Although the number of wounds in this series was comparatively small—in fact, too small for most individual surgeons to attain experience and skill comparable to that developed by surgeons during the late world war—this has in part been compensated for by devoting more time to individual cases and by being able to follow them through personally. However, although experience in Malaya has confirmed the soundness of the principles of wound surgery developed during the second world war, there have been certain developments since which are of importance. These are:

(1) Under present conditions in Malaya, with penicillin available in sufficient dosage and supplemented if necessary by the newer antibiotics, wound infection can be so greatly retarded as to make the time element, from this aspect, no longer important. Under favourable conditions serious wound infection should be almost eliminated.

(2) Some wounds are of course lethal, killing either immediately or very soon after wounding. There is little that can be done about these except to try to reduce their incidence by good battle-training and possibly by some form of protection such as the laminated nylon vest. The great majority of deaths from wounds, not of themselves necessarily lethal, occur directly or indirectly from haemorrhage. This must be regarded as a preventable condition, and efforts to reduce mortality from missile wounds can be directed with much profit along these lines. The three main life-saving procedures in such cases are adequate first aid to limit bleeding from accessible sites; quick adequate blood replacement for cases with oligaemic shock, actual or imminent; and speedy evacuation to a surgical centre of any case with inaccessible bleeding. There is nothing new about these fundamental principles; nevertheless, many of the deaths in the series under review were due either to failure or to inability to apply them. They cannot be restated too often.

(3) Helicopter evacuation has come to stay. It will not always be available, because we are unlikely always to have the local air superiority essential for the operation of these vulnerable aircraft. When they can be used, however, they are life-saving and should be the normal method by which penetrating wounds of the head, spine, chest, and abdomen, maxillo-facial wounds, and those involving the femur or major vessels are evacuated. Apart from the time saved and the minimization of shock while in transit, they have the tremendous advantage that, once airborne, they can cover considerable distances quickly and so enable serious cases to be operated on well in the rear, where adequate surgical and nursing facilities can be provided and the need for subsequent speedy evacuation is less urgent.

Any report on war surgery in Malaya would be incomplete without a tribute to all ranks of the Army Medical Services responsible for the management of these cases. Despite constant shortages of staff which necessitated long hours of work, their efforts have been tireless, and the fact that the results obtained are the best in the history of the British Army is entirely due to the high quality of their team-work. In particular we have been indebted to the junior surgeons and anaesthetists, without whom it would have been impossible to carry on.

Summary

Missile wounds in 774 casualties sustained during a three-year period in Malaya are reviewed. The mortality among cases alive on admission to hospital was 5.5% and among cases fit for surgery 3.7%.

Management of wounds followed the principles developed during the second world war and confirmed their soundness.

The causes of death are discussed and suggestions made for reducing them.

I am indebted to Brigadier C. W. Greenway, Director of Medical Services, Far East Land Forces, for permission to send these notes for publication.

SPEECH AFTER REMOVAL OF UPPER END OF OESOPHAGUS AND THE LARYNX

BY

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The disease generally known as post-cricoid carcinoma usually arises on the upper surface of the cricopharyngeal fold at the mouth of the oesophagus. The incidence is, unfortunately, of sufficient frequency to present a serious problem in treatment. The growth tends to infiltrate the back of the larynx and is usually far advanced before compelling the patient to seek advice; its progress is such as to inflict great suffer-

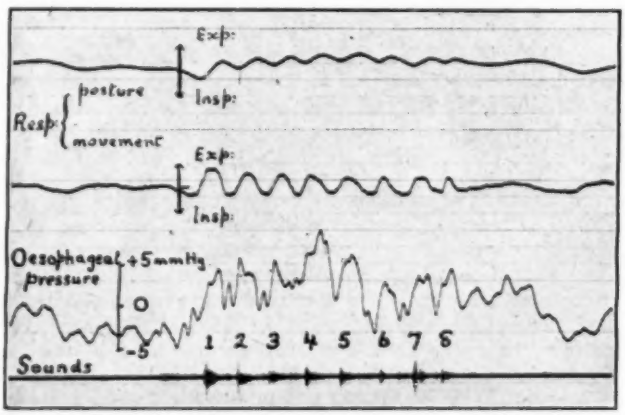
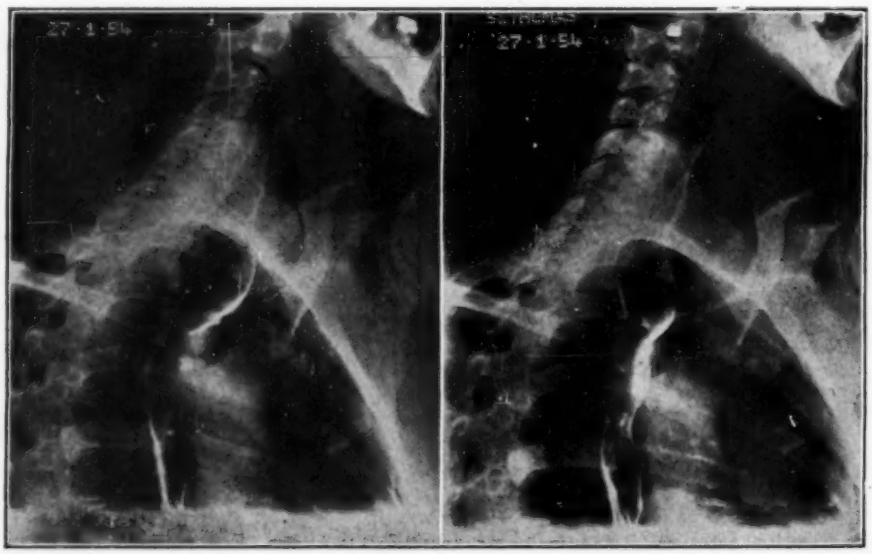


FIG. 1.—Recording of respiratory movements, oesophageal pressure, and sounds while patient counts up to eight. Each sound occurs as the oesophageal pressure rises during a sharp expiratory movement.



A B

FIG. 2.—Upper part of oesophagus and the reconstituted pharynx, showing the falling together of the anterior and posterior walls at about the upper limit of the graft. A, during speech. B, after speaking. The junction of skin tube and oesophagus is widely open during speech; the skin tube is distended by escaping air.

ing, because of difficulty in swallowing, pain, cachexia, and changes in the voice, sometimes with difficulty in breathing.

Many years of sad experience have emphasized the necessity for drastic treatment if the patient is to be spared a slow and distressing death. Several conclusions have been reached. They are that irradiation is ineffective; that limited operations, with preservation of the larynx, are very rarely effective; and that removal of the upper end of the oesophagus must be accompanied by excision of the larynx, with part of the pharynx. The complete operation should be performed at the earliest possible moment after establishment of a diagnosis, before the progressively infiltrating growth has further opportunities of spreading. The operation must be truly radical, with block dissection of glands, complete or partial according to distribution of the primary growth or metastases. And, finally, immediate restoration of the food passage should be attained, the method adopted being the introduction of a specially shaped tube of rubber or plastic material, covered with a split-thickness skin graft.

It is well recognized that strictures may subsequently occur, but their relief does not present undue difficulties if a suitable plastic operation is performed. Objections to radical operation have in the past been based on the immediate dangers, on the probability of recurrence, and on the loss of speech. Even if the drastic one-stage procedure advocated is adopted the operative mortality should be slight; the prospects of cure are sufficient to afford a reason for its performance. The possibility of speech is illustrated by the following case.

Case Report

A woman aged 46 at the time of operation five years ago was subjected to the method described; while retaining a plastic tube through which she swallowed, she led an active life and drove her motor-car vigorously. Stricture formation at the junction of skin tube and oesophagus required plastic repair, carried out by Mr. Moore, plastic surgeon to King's College Hospital. She now takes ordinary meals, although requiring a drink of water at times to assist the passage of food through the non-muscular skin tube. Lessons in speech education were given by Miss Swallow, but full credit must be given to the patient herself for her determined and prolonged efforts to talk, with so successful a result that she can converse freely and is easily understood even on a telephone. At a meeting of the Association of Plastic Surgeons in February, 1953, the patient was audible at the back of the hall (Negus, 1953).

Comment

Investigation of the mechanism of speech has been carried out by the method of Bateman, Dornhorst, and Leathart (1952). It appears, from the records obtained, that her speech is essentially similar to that after simple laryngectomy (Fig. 1), except that the production of sound is at the junction of skin tube and pharynx where the anterior and posterior walls fall together, and not at the level of the crico-pharyngeal sphincter, the latter having been completely removed at operation. Radiological examination while swallowing barium showed a sufficiently wide food passage at all levels; the narrowing visible in the film reproduced here (Fig. 2) seems to depend on contraction of the remaining fibres of the pharyngeal constrictor muscle, and offers no impediment to the passage of food. Although during normal breathing the oesophagus contained air, the narrowing was enough to prevent free oesophageal respiration, and, during the expiratory efforts of speech, sufficient resistance was presented to outgoing air to allow the production of sound. The patient had an advantage over one with a simple laryngectomy in that no special knack of filling the oesophagus with air had to be acquired, and she herself said that all she had to do to make a sound was to attempt to shout.

It may be that the exact form of the graft which allowed sound production was a fortunate chance. Further patients will have to be examined to check this. If necessary, there should be no insuperable difficulty in imitating in others the anatomical features found in this patient.

We feel that the demonstration of efficient speech in this patient should be an encouragement to others, and an indication that with sufficient application the acquisition of a voice is a possibility.

We thank Dr. Gordon Gryspeerdt for radiological help.

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A PLASTIC SURGICAL DRESSING

BY

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The rising costs of gauze and absorbent wool have stimulated a search for an alternative dressing for surgical and other wounds. The object of this paper is to record our experiences with a liquid plastic dressing (" nobecutane "), which is an acrylic resin dissolved in a mixture of acetic esters (Hogeman and Olow, 1953). This dressing has been the only covering for 200 clean surgical wounds.

Method of Application

At the conclusion of the operation, after the last skin suture has been tied, the wound is wiped clean and then dried with a dry gauze swab. The plastic is applied with a brush, a plastic applicator, or a spray. A film forms over the whole wound and dries in about three minutes; the patient is then ready to return to the ward. About 2 to 3 ml. of the liquid plastic has proved to be sufficient for the average abdominal incision. Provided that the wound is adequately covered, a thin layer is preferable to a thick one. We found the spray to be the most convenient method of application and the most economical. The plastic applicator provided a satisfactory alternative, but application with a brush was too wasteful, and with this method 10 ml. was required for an incision 6 in. (15 cm.) long.

The plastic forms an elastic, transparent, and adherent dressing which remains in position until the skin sutures need removal. It is then peeled off with forceps and the sutures are removed in the usual way. In some of our cases we applied the plastic to the skin of the operation site before operation and then operated through it, making a further application at the conclusion of the operation. This was unsatisfactory, because portions of the plastic film tended to flake away from the skin edge and fall into the incision.

Disadvantages

In the liquid state this plastic is inflammable, but not once it has dried as a film over the wound. It is painful

when applied to unanaesthetized raw surfaces. Absolute haemostasis is essential; oozing from the wound strips up the plastic film. When it is necessary to drain a wound a gauze-and-wool dressing should be applied to the area near the drain, but the rest of the wound can be dressed with the plastic. Another minor disadvantage is that the plastic will not adhere to a wet surface. The removal of sutures is slightly more painful than with a conventional dressing, as the ends of the suture may catch in the plastic; if a continuous skin suture is used this objection does not apply. At first we applied too much dressing, with the result that a thick film formed over the wound; we now use less of the liquid, and the film which results interferes very little with the removal of skin sutures.

Advantages

The dressing can be easily applied and maintained. If it wears thin or cracks a second application of the plastic spray can be made by the ward nurse. It is transparent; therefore the wound can be inspected with ease. It is permeable to air and water vapour but impermeable to bacteria; the wound does not become moist or macerated. The dressing can be washed with soap and water; this makes it possible for the patient to take a bath days before the sutures are ready for removal. It is flexible and strong, with the result that the patient can move freely not only the thorax and abdomen during respiration but a joint such as a hip, even when the incision crosses the joint line. In our experience patients with wounds dressed in this way are more comfortable than those with conventional dressings, and after an initial period of qualified scepticism our ward sisters prefer the plastic dressings. The dressing is not irritant, and only one of the 200 wounds in this series became infected; this settled rapidly after removal of the sutures. The solution has remained sterile in its bottle or spray container during routine use in the ward and operating theatre.

The plastic film is strong and capable of withstanding considerable strain; it has not fragmented or cracked before removal of the skin sutures in any of our patients, but we have used it only on in-patients. It has been found to be of special value as a dressing for wounds of such regions as the face or scrotum, where it is difficult to hold a gauze-and-wool dressing in position; but we use it as a routine for all clean surgical incisions. The plastic actually holds the skin edges together, with the result that tension is reduced and healing appears to be more satisfactory. We have not had the opportunity of applying the plastic to the skin near to an intestinal fistula, but it provides a satisfactory dressing for the incision near to a colostomy.

Of particular importance is the cost. This plastic sells at 0.84 of a penny per ml.—2½d. for the average abdominal incision. A gauze-and-wool dressing held in position by ½-in. (1.25-cm.) adhesive strapping also costs about 2½d. for a similar incision, but it has to be renewed at least once during each patient's stay in hospital. In our view the use of this plastic should reduce the cost of dressings for clean surgical incisions by at least 20%, and it saves the staff much time and trouble.

Conclusions

This liquid plastic appears to have advantages over conventional gauze-and-wool dressings and other plastic substances.

Its special advantages include easy application, cheapness, easy wound inspection, increased comfort for the patient, and less work for the nursing staff.

Its main disadvantages are that haemostasis must be complete, although time spent achieving this rarely harms the patient. Also, the removal of sutures is made more difficult if too thick a layer of plastic has been applied.

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SUXAMETHONIUM SENSITIVITY IN HEALTH AND DISEASE

A CLINICAL EVALUATION OF PSEUDO-CHOLINESTERASE LEVELS

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Suxamethonium chloride (succinylcholine chloride; "scoline") has an established place among the synthetic compounds which have been introduced to produce muscle relaxation during anaesthesia. Immediate and absolute muscular relaxation, flexible and easily graduated effect, associated with rapid recovery and absence of secondary actions, satisfy many of the criteria of an ideal drug.

Disturbing reports have appeared, however, of unexpectedly prolonged action following therapeutic doses. It has been established that the drug is hydrolysed by serum pseudo-cholinesterase (Ps.ChE.), and Bourne *et al.* (1952), Evans *et al.* (1952a), and Bourne (1953) found low Ps.ChE. levels in the sera of patients showing delayed recovery. Bourne (1953) suggested that the dose should be regulated by body weight, citing the work of Thesleff (1952), and thought that in "frail" patients this dose should be reduced. Evans *et al.* (1952b) demonstrated an inverse relationship between this Ps.ChE. level and the duration of action of the relaxant, and later the same authors (1953) found that injections of a purified Ps.ChE. shortened this action. They advised against giving suxamethonium to patients likely to have a low serum Ps.ChE. level such as may be found in anaemia, liver disease, and after poisoning with insecticides and war gases. Lehmann (1952) thought that the use of the drug would be safe if these patients and those suffering from malnutrition were excluded from treatment. Macintosh (1953), however, found that undernourished and anaemic Asians showed no greater susceptibility to the drug.

During employment of suxamethonium in abdominal surgery, it seemed that the responses encountered, especially among anaemic patients, were not altogether in accordance with the suggested criteria. It appeared necessary to re-examine the clinical factors concerned. This investigation, therefore, was to consider the relationship between Ps.ChE. levels, body weight, and duration of action of the drug, and to determine whether exclusion from treatment of any particular condition, particularly anaemia, was warranted. This paper presents the association found between clinical fitness, Ps.ChE. levels, and suxamethonium sensitivity, and the conclusions drawn therefrom.

Material and Methods

The haemoglobin and Ps.ChE. levels were estimated in 114 patients (56 female, 58 male) from the adult surgical wards before operation. No selection was made except to exclude patients suffering from liver disease or clinical malnutrition, and, owing to technical difficulties, some emer-

gency admissions. The conditions from which these patients suffered, in groups of clinical health (Saklad, 1941; Nosworthy, 1943), are shown in Table I.

TABLE I.—*Clinical Conditions and Operative Procedures of 114 Patients Taken at Random Except for the Exclusion of the Conditions Specified in the Text*

Operation	Clinical Condition			
	Good	Fair	Poor	Serious
Gastric	5	4	7	4
Other abdominal	5	11	4	4
Genito-urinary	9	8	7	1
Herniorrhaphies	5	1	1	1
Other	28	7	1	1
Total ..	52	31	20	11

The duration of apnoea following suxamethonium administration was accurately measured on many occasions. Adult patients were anaesthetized with from 0.2 to 0.25 g. of intravenous thiopentone and were stabilized on nitrous oxide, 5.5 litres a minute, and oxygen, 2.5 litres a minute, before the intravenous injection of suxamethonium, 0.7 mg. per kg. body weight. During the apnoea controlled respirations at a rate of 12 to 15 a minute were maintained with a mask and manual inflation of the rebreathing bag.

The haemoglobin was estimated by the alkaline haematin method (King, 1951), using a photoelectric colorimeter and corrected to a scale in which 100% equalled 14.8 g. haemoglobin per 100 ml. of blood.

The Ps.ChE. estimations were performed with the colorimetric method described by Huerga *et al.* (1952), which is based on the hydrolysis of acetylcholine bromide in a buffered solution under standard conditions. The results are expressed in micromols of acetylcholine bromide hydrolysed per hour per millilitre of serum. This technique is simple compared with previous methods which require accurate *p*H measurement or Warburg gas analysis, and comes within the scope of any hospital biochemical laboratory. A single emergency result is available in one and a half hours. Our coefficient of deviation of duplicate tests was ± 1.4. These Ps.ChE. estimations were undertaken by one of us (J. H.) at the Central Laboratory, Portsmouth.

Huerga found that the values in 132 normal individuals ranged from 130 to 310 micromols : in the present investigation the values in 60 healthy individuals varied between 135 and 280 micromols.

Suxamethonium chloride (" scoline ") was used in all cases.

Results

Influence of Ps.ChE. Levels on Duration of Effect.—The duration of apnoea was plotted against the Ps.ChE. level for 31 subjects (Fig. 1). It confirmed the inverse relationship described previously.

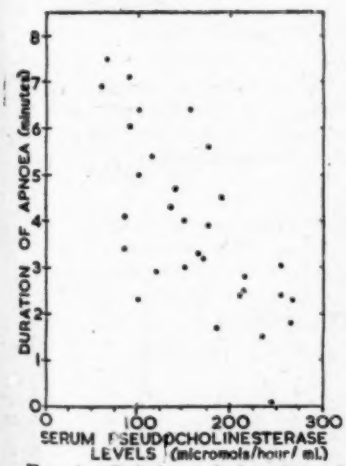

FIG. 1.—Relation of duration of apnoea following suxamethonium (0.7 mg. per kg. body weight) to serum pseudo-cholinesterase level.

The Dose/Body-Weight Relationship.—The duration of apnoea was measured in 118 adult patients receiving 0.8 to 1.3 mg. per kg. body weight (Fig. 2), and in 50 adult patients receiving 0.7 mg. per kg. body weight (Fig. 3). It confirmed that in adults an increase in dose produces an increase in action (Bourne, 1953; Thesleff, 1952). In small children it appears that comparable doses based on body weight have a shortened action. Further work is being done in this respect, and a possible explanation is discussed later.

Range of Ps.ChE. Levels in Pre-anaesthetic Patients.—Fig. 4 represents the incidence of Ps.ChE. levels in the 114 unselected patients. Compared with the normal range of 130 to 310 micromols/hour/ml., subnormal levels were found in 19% of patients. Table II shows the clinical conditions encountered in the 22 patients with subnormal levels. Nineteen were classified as " ill," ten of these as " serious "; three came within the " fair " group, but these suffered from conditions requiring semi-urgent or urgent admission to hospital. In the ill patients no obvious correlation could be found between the subnormal levels and the diseases

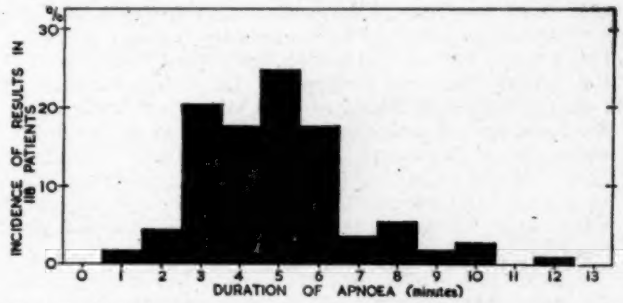

FIG. 2.—Relation of duration of apnoea to dose of suxamethonium (0.8–1.3 mg. per kg.)

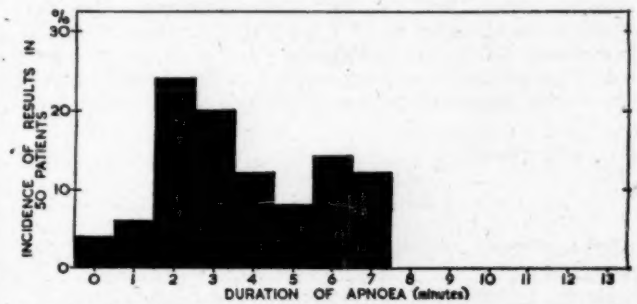

FIG. 3.—Relation of duration of apnoea to dose of suxamethonium (0.7 mg. per kg.)

present. Although anaemia was present in 12 patients in this series and its incidence is significantly higher than in the healthier groups, it should be noted that when the whole series (114 patients) was considered 48% of those with unsatisfactory haemoglobin levels—that is, less than 80%—had normal Ps.ChE. levels. Exclusion from treatment with suxamethonium of these patients on the grounds of anaemia alone would have been unjustified.

Relationship of Haemoglobin to Ps.ChE. Levels.—The Ps.ChE. levels were plotted against the corresponding haemoglobin percentages (Table III). Although a general relationship was apparent, a very wide scatter occurred. Of the patients with a haemoglobin content over 80%, subnormal Ps.ChE. levels were found in 10%; these cases might have been accepted as safe (Lehmann, 1952), when in fact subnormal Ps.ChE. was present. The few patients with haemoglobin values below 40% were all found to have Ps.ChE. levels within the normal range. In spite of the significant correlation

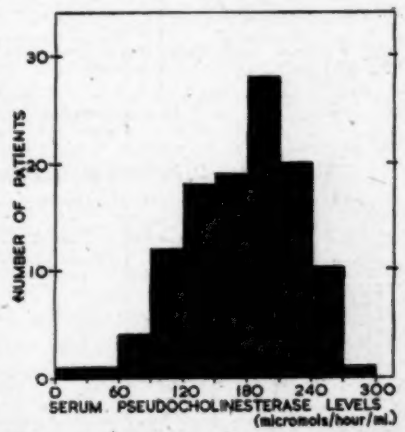

FIG. 4.—Incidence of serum pseudocholinesterase levels in 114 pre-operative patients.

present between these two values (correlation coefficient= +0.47), the enzyme level found for each 10% range of haemoglobin content showed that in these 114 patients the presence or absence of anaemia was an unreliable index of the Ps.ChE. activity owing to the wide ranges occurring.

Relationship of Clinical State to Ps.ChE. Levels.—It became clear during analysis of these results that there was a relationship between the Ps.ChE. level and the clinical health groups into which the patients had been classified (Table IV). No low levels were found in the obviously clinically healthy and, although fewer patients were observed in the lower grades of health, the increased incidence therein of low enzyme levels became significant. Of the seriously ill patients 81.8% had subnormal levels, while the two patients with levels within the normal range were at the lowest limits of normality. Of those classified as "poor" 50% were found to have subnormal levels, while the remainder all fell within the lower third of the normal range. When more crudely grouped as "ill" and "healthy" 61.3% of the former, but only 3.6% of the latter, were subnormal. Examined statistically a very high degree of significance between these two groups is obtained ($P = <0.01$).

A further 18 patients who were selected as coming within the two lower health groups were studied. Of these ("poor" 7, "serious" 11), 14 were within the subnormal range of Ps.ChE. levels and three were within the lowest normal range (130, 138, and 138 micromols). The last patient was classified as poor as she suffered from toxaemia associated with a septic abortion. Her high Ps.ChE. level of 198 micromols was unexpected, but she showed unusual powers of recovery and was discharged within seven days.

TABLE II.—*Diseases Found in Patients Who Had Subnormal Serum Ps.ChE. Levels*

Sex	Age	Primary Condition	Secondary Condition	Hb %	Health Group	Serum Ps.ChE. Level*
M	42	Empyema	Toxaemia	81	Serious	10
F	62	Carcinoma (gastric)	Haematemesis	64	"	50
F	50	" (sigmoid)	Melaena	68	"	60
M	81	Retention of urine	Uraemia	64	Poor	63
F	43	Obstruction (large bowel)		64	Serious	73
M	54	Carcinoma (gastric)	Debilitation	45	"	88
M	63	Appendix abscess		86	Fair	90
F	44	Gastric ulcer	Haematemesis	66	Serious	90
M	60	Abdominal investigation	Depressive psychosis	110	Fair	92
M	75	Enlarged prostate	Haematuria	46	Poor	98
M	64	Gastric ulcer	Enlarged prostate	63	"	98
M	62	Carcinoma (gastric)	Haematemesis	53	Serious	100
M	59	" (sigmoid)	Hydronephrosis	68	"	100
F	26	Thyrotoxicosis		79	Fair	100
F	50	Carcinoma (cervix)	Post-radiotherapy	80	Poor	103
F	60	Obstruction (small bowel)	Abdominal secondaries	95	"	105
M	83	Retention of urine	Coronary thrombosis	86	Serious	113
M	64	Gastric ulcer	Jejunostomy	88	Poor	119
F	48	Gummatous infiltration of peritoneum		57	"	120
F	32	Tuberculous pyonephrosis		87	"	123
M	18	Acute appendicitis	Pulmonary phthisis	98	"	125
M	67	Gastric ulcer	Haematemesis	35	"	130

* In micromols/hour/ml.

TABLE IV.—*Relation Between the Clinical Condition of a Patient and the Serum Ps.ChE. Level*

	Clinical Condition of Patient				Total
	Healthy		Ill		
	Good	Fair	Poor	Serious	
No. of cases with normal Ps.ChE.	52	28	10	2	92
No. of cases with subnormal Ps.ChE.	—	3	10	9	22
Percentage in clinical groups with subnormal Ps.ChE.	0	9·7	50	81·8	19·3
	3·6		61·3		
Range of Ps.ChE. values in each clinical group	135–275	90–265	63–180	10–145	10–275
Mean and standard deviation in each group	207±34	175±38	128±26	93±37	173±53

Clinical groups.—Good:—No organic or pathological condition present; or patients in whom a pathological condition is localized and does not cause any systemic disturbance or abnormalities. Fair:—A moderate but definite systemic disturbance caused either by the condition that is being treated or by other existing pathological processes. Poor:—Severe systemic disturbances from any cause or causes (no fixed criteria)—for example, combination of cardiovascular and respiratory disease that severely impairs normal function. Serious:—Extreme systemic disorders that already threaten life regardless of treatment.

Discussion

Little can be gained by a study of most published reports of prolonged action which have been attributed to suxamethonium; many do not bear critical examination. Following an early warning (Gould, 1952) reports appeared (Harper, 1952; Hewer, 1952; Hurley and Munro, 1952; Love, 1952) in which a prolonged effect apparently followed therapeutic doses. A wide variety of explanations were suggested, although Foldes (1952) thought that the patients were overdosed. Owing to the lack of biochemical evidence it is difficult to dissociate the superadded effects of hyperventilation and of reflex laryngeal apnoea from local stimulation of endotracheal tubes.

A low Ps.ChE. level was found by Bourne (1953) in five patients who had a moderately prolonged action. Further cases were reported (Day, 1952; Grant, 1952; Hodgson and Kothari, 1952; Mackay, 1952; Ruddell, 1952). In none of these cases was a Ps.ChE. estimation available. In the discussion that followed, Durrans (1952) thought that a case had not been made out against suxamethonium as the causative agent in the prolongation of apnoea, and believed that thiopentone was responsible in the majority of cases.

Barron (1952) claimed that large doses of nikethamide terminated the apnoea, but in patients in whom this is due to a low Ps.ChE. level it is difficult to visualize the mechanism involved. It suggests that superadded apnoea from central respiratory depression was present. Nosworthy (1953) stated that blame for unexpected prolongation was often laid on the last drug given, with a failure to distinguish between central and peripheral effects.

There would seem to be little doubt that a pseudopotentiation of apnoea can be produced by acapnia, reflex laryngeal stimulus, overstimulation of the Hering–Breuer reflex, central respiratory depression, and other factors not altogether excluded in many of these reports.

TABLE III.—*Relationship of Haemoglobin Content and Serum Ps.ChE. Level in 114 Pre-operative Patients*

Hb Group %	Ps.ChE. Range	Ps.ChE. Mean	Ps.ChE. Scatter Diagram (micromols/hour/ml.)												Total No. of Cases
			0–	25–	50–	75–	100–	125–	150–	175–	200–	225–	250–	275–	
101–	92–265	200	—	—	—	1	—	3	3	2	5	5	4	—	23
91–	105–275	188	—	—	—	—	2	5	6	14	7	4	2	1	41
81–	90–255	173	—	—	—	1	3	2	4	3	6	1	1	—	21
71–	10–230	141	1	—	—	—	2	4	1	1	1	1	—	—	11
61–	50–193	106	—	—	3	2	1	—	—	2	—	—	—	—	8
51–	63–180	123	—	—	1	—	1	—	1	1	—	—	—	—	4
41–	88–135	107	—	—	—	2	—	1	—	—	—	—	—	—	3
31–	130–190	157	—	—	—	—	—	1	1	1	—	—	—	—	3
Total ..	10–275	173	1	0	4	6	9	16	16	24	19	11	7	1	114

Correlation coefficient = +0·47.

The incidence of true prolongation is difficult to establish. It occurs when a low-level Ps.ChE. subject receives a "relative overdose." Early in a personal series of over 2,000 patients to whom suxamethonium had been administered several cases of moderate prolongation of 10 to 15 minutes occurred, but in only two was this time exceeded (Hodges, 1953a). They were confirmed as true "long reactors" having depressed Ps.ChE. levels.

If it is accepted that depressed Ps.ChE. activity is the explanation of most true sensitivity it is salutary that the results of those workers who have examined this activity in health and disease should be studied.

In Health.—Normally the individual Ps.ChE. level remains remarkably constant over long periods, unaffected by physiological changes (Vahlquist, 1935), menstruation (Hall and Lucas, 1937), or seasons of the year (Callaway *et al.*, 1951), though geographic and climatic variations have been suggested (Lackay and Slaughter, 1942; Forbat *et al.*, 1953). Sexes show an even distribution; McArdle (1940) found the levels slightly raised in a small series of children. Organo-phosphorus insecticides and therapeutic radiation (Barnard, 1952) cause a depression, and a fall follows the infusion of albumin (Vorhaus *et al.*, 1950). It may be noted here that suxamethonium when administered to children based on a dose/body-weight relationship, normally adequate in adults, often needs to be supplemented. This apparent tolerance supports the findings of McArdle (1940).

In Disease.—Among pathological states held responsible, hyperpyrexia (Antopol *et al.*, 1937), acute infectious diseases (Hall and Lucas, 1937), cardiac failure, uraemia (McArdle, 1940), and catatonia (Tod and Jones, 1937) were found to depress the Ps.ChE. level, while thyrotoxicosis, diabetes, and anxiety states caused an elevation. In malnutrition (Waterlow, 1950; Hutchinson *et al.*, 1951), in anaemia (Faber, 1943; Scudamore *et al.*, 1951), and in parenchymatous liver disease (Vorhaus *et al.*, 1950) low levels were found in a large percentage of patients.

In the present series the findings did not suggest that such abnormalities existed constantly in the conditions mentioned. Such patients have been anaesthetized on many occasions, using a suxamethonium technique without incident.

Association Between Low Levels and Clinical State

This association has been noted by several observers. Diseases which "essentially affected the general condition" reduced the Ps.ChE. level (Faber, 1943), which level, though it might be used as a critical index of liver function, was of most value when considered in conjunction with the clinical findings (McArdle, 1940). The low levels found in anaemias followed and reflected clinical changes (Scudamore *et al.*, 1951), while in undernourished infants the level rose as their general state improved (Waterlow, 1950). In adult malnutrition the rise due to increased feeding was not related to the increased consumption of any of the major dietetic constituents but rather to a gradual gain in well-being (Hutchinson *et al.*, 1951).

Low levels were found in advanced tuberculosis and carcinomatosis (Vahlquist, 1935; Jones and Stadie, 1939), while Milhorat (1938) found that depression of Ps.ChE. activity occurred in the chronically debilitated state following advanced and toxic processes in a wide variety of conditions; this was not normally characteristic of the diseases when encountered in the early stages. He found that in confined disease with no general manifestations only moderate depression occurred, even in "fatal" illnesses. Milhorat agreed with others (Lucas *et al.*, 1935; McGeorge, 1937) that depression of Ps.ChE. activity could not be related to any particular disease, and Augustinsson (1948) stated that "the mass of data . . . did not allow of any conclusions."

During the present investigation the haemoglobin content was not found to be a reliable guide to Ps.ChE. activity when considered apart from the clinical condition of the patient. Some patients who were in relatively good health apart from a severe anaemia were found to have normal Ps.ChE. levels, while extremely low values were found in patients with normal haemoglobins.

The association between clinical health and Ps.ChE. activity was very obvious in this study, where a majority of "ill" patients had low levels irrespective of the disease prevailing. The evidence here presented does not justify an arbitrary exclusion *en bloc* from the advantages of suxamethonium treatment, where indicated, of anaemic patients or those suffering from any particular diseases, on the grounds that a low Ps.ChE. level is likely to occur. A more reliable method of estimating this value is a careful clinical assessment, the degree of impairment of clinical health being the overriding factor. In certain apparently normal people the Ps.ChE. may be depressed below normal limits (Davies, 1952; Forbat *et al.*, 1953), though these must be extremely rare. Judging by the response to treatment, no such patient has been encountered in our 2,000 cases.

Seriously ill and debilitated patients are the most likely to show depression of Ps.ChE. activity, but it is in these patients that great benefit is likely to result from the use of suxamethonium. One of us (R. J. H. H.) does not consider that a suspected, or confirmed, subnormal level is any contra-indication to the use of the drug provided that the administration is on a rational basis. Pre-operative clinical assessment, aided if need be by biochemical analysis, together with the use of test doses (Bourne, 1953) and dilute solutions (Bromage, 1953), should reduce the incidence of unexpected difficulty to insignificant proportions. A wider understanding of the factors concerned in depression of Ps.ChE. activity has latterly enabled many anaesthesias on potential "long reactors" to be conducted successfully. The majority of low-level subjects found in this investigation had suxamethonium administered by intravenous drip throughout long procedures. In these subjects complete operations can sometimes be performed safely, using a total dose of the drug that has been advocated as suitable for the induction of paralysis: doses as low as 60 to 100 mg. per hour are not uncommon, though 1,100 mg. per hour has been needed on occasion (Hodges, 1953b) in some normal patients.

The reactions of patients should be judged at the time of administration, a small dose for endotracheal intubation being convenient. Reviewing the synthetic relaxants, Foldes *et al.* (1952) state that suxamethonium "should be the first choice when the use of a muscle relaxant is indicated, especially so in the old or poor-risk patient." We believe this to be so, but due regard must be paid to the sensitivity of these patients. Although forms of prepared Ps.ChE. ("cholase") may become available for the resuscitation of patients overdosed, avoiding the necessity for an antidote is a more rational, more satisfactory, and safer procedure.

Summary

Unexpected prolongation of effect following administration of suxamethonium (succinylcholine) is due primarily to a low serum Ps.ChE. An inverse relationship exists between the duration of effect and the individual Ps.ChE. level.

Subnormal Ps.ChE. levels were found in 19% of pre-operative patients; the majority of these low-level patients were clinically "ill."

The reported cases of prolonged action following the use of suxamethonium, and the literature on the variations in Ps.ChE. during health and disease, are reviewed.

No reliable correlation was found between the subnormal levels, anaemia, or any particular disease, but the Ps.ChE. level appears to be a critical index of the general physical state.

The pre-operative assessment of the degree of impairment of general health was the most reliable guide to low Ps.ChE. levels and therefore to the probable suxamethonium sensitivity of the patients.

Neither particular diseases nor subnormal levels *per se* are contraindications to the use of suxamethonium, which is regarded as the drug of choice among the relaxants at present available.

In anaesthesia no dose of suxamethonium can be preconceived with certainty. The rational use of dilute solutions allows each patient to be assessed empirically at the time of administration.

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The world's lowest mortality from tuberculosis for the whole of 1953 was recorded in the Netherlands, according to the World Health Organization's *Epidemiological and Vital Statistics Report No. 5 (1954)*: it was 9.2 deaths per 100,000 population. Denmark was the next most favoured country, with 9.6 for all of 1953, but led the world with the lowest tuberculosis mortality ever registered, i.e., 5.2 per 100,000 population, which was maintained for two months—July and August, 1953. While the Netherlands and Denmark were alone in achieving last year this remarkable position, all of the 25 countries studied in the W.H.O. report have registered considerable gains in the struggle against tuberculosis, and show definite progress over the situation as reported for 1950 in a previous W.H.O. study. These 25 countries, selected from five continents, are the only ones able to provide valid and comparable health statistics, and the situation with regard to tuberculosis is without doubt far from satisfactory in the countries which do not offer reliable statistical information. In fact, even in the group of countries studied by W.H.O., mortality rates from tuberculosis as high as 150 per 100,000 population were recorded in 1953 in some places.

FOOD-POISONING AT SEA

BY

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Passenger ships on long voyages are isolated close communities which are subject to outbreaks of enteritis or gastro-enteritis. As an outbreak is usually under control before the ship arrives at her destination, the port health authorities have no reason to investigate the matter further. The evidence is stale, the data are often insufficient, and the community breaks up as the ship docks. Very rarely is there any publicity.

In some ways a ship at sea makes an ideal experimental group. The crew have free medical attention, and, given confidence in their medical officer, will report sick early, especially with a little advance propaganda. The passengers, bored with their enforced idleness, eagerly seek a new topic for complaint. In fact, there is likely to be almost 100% accuracy in the number of cases recorded. All sources of food and routes of service are easily traced. All the same, unless thorough investigation is made at the outset, trails are lost owing to the complexity of organization.

Epidemic intestinal disease presents gastric or enteritic symptoms which may be acutely explosive or so mild as to be little more than a temporary embarrassment. Cases have been described in which the acute explosive vomiting has caused immediate collapse. On the other hand, I have attended patients who have had nothing but a repeated bowel action with only partial control and almost no warning.

On shore it is customary to attack an epidemic with a clear bacteriological picture available. As laboratory facilities are rare at sea the bacteriology is almost always a matter of speculation based on the clinical evidence. In fact, the medical officer must adopt a rationalized version of the purely clinical practice of former years and identify the bacterium or other cause from the symptoms observed.

Catering Services on Board

To understand the channels of infection it is necessary to know something of the layout and organization of the catering services in a large passenger ship: without a clear picture it is not possible to appreciate the reason for certain apparent anomalies in the spread of epidemic conditions.

The ship must be considered as two separate sections: the ship proper, manned by a crew of seamen and engine-room personnel; and, separated by material and disciplinary barriers, the hotel-type organization of cooks and stewards caring for the passengers of one or more classes and for the ship's officers. The ship's company has its own kitchen (or galley), served by a certificated ship's cook and his assistants. Here all food for the crew is prepared from raw provisions, except for bread, cake, puddings, ices, and sweets, all of which come from a single bakery (with a staff of bakers separate from other food preparers), which serves the whole ship with a full range of bakers' products according to the requirements.

The water for all departments is supplied from common storage-tanks, and is potable water passed through filters and pumped up to high-level gravity supply tanks, whence it passes to all the taps in the ship. The water-tanks are filled up at convenient ports: there is no provision for distilling drinking-water on board from sea-water (except

for a small emergency apparatus), as the process is much too expensive.

The stewards, cooks, passengers, and officers are fed from one (or more) passenger galleys: all the officers eat with the passengers, except the engineer officers, who have their food served in a separate mess-room. The stewards are also fed in a separate mess-room, though many eat in odd places, often standing to their meals. The cooks may keep back food for themselves in their utensils, though usually they eat special titbits which they prepare according to their fancy.

Provisions for the crew galley and passengers' galley are distributed from common refrigerated meat, fish, and vegetable stores and "dry" store-rooms. The bakery draws its special provisions from the same stores. The galleys prepare meals as far as the sweets: these last come from the baker. The ship's company mess-boys collect their relatively simple fare from the crew galley door: the elaborate passenger menus require special serving-rooms with hot plates and similar devices. These pantries (and stillrooms) are the focal point of the various articles of foods—salads, cold dishes, hot dishes, puddings, ices, cold and hot drinks, fruit, and so on. It is here that they are subject to the maximum handling prior to serving and to much transfer from one dish to another. From here the food and drink are distributed to the passengers and officers, to the engineer officers (via a sub-pantry), and to the stewards.

Washing up is done in the pantries in the passenger accommodation: the crew mess-boys wash up in their messes. There is no refuse problem, as all waste and garbage is thrown overboard at once.

Briefly, then, the ship's crew and the passengers, officers, and their attendants have separate sources of cooked food but a communal bread and water supply: there is no fresh milk on board except for a small stock of sterilized milk provided for infants.

Gastro-enteritis a Familiar Feature

As gastro-enteritis due to food-poisoning is not a notifiable complaint to the port health authority statistics are few. All ship surgeons appear to be familiar with the condition, and it seems to be accepted as a normal feature of ship-board life. Often the condition is mentioned as endemic: indeed, so much is this so that the general attitude is one of resigned vigilance following upon an initial enthusiastic but unsuccessful attack on the first outbreaks. Unfortunately, there is no concise and accurate account of the condition in which the clinical and bacteriological aspects of the question have been co-ordinated with modern practice in public health and naval hygiene.

Royds Jones (1938), describing outbreaks aboard a passenger ship, divided them into three categories: (1) sporadic cases among passengers and crew during a voyage usually on entering or leaving a hot and humid climate; (2) sporadic cases caused by eating ashore; and (3) acute epidemics, often affecting only a section of the community on board.

Details of an Outbreak

An outbreak persisted in a large passenger steamship throughout the passage from Japan to Britain in the winter of 1946–7. There were 52 cases. The ship, with a crew of 300 and some 250 passengers as well as 2,800 troops, travelled from Japan via Shanghai, Hong Kong, Singapore, Bombay, and the Suez Canal to Southampton, and so was exposed to a range of a climate from the bitter cold of continental China to the extremes of equatorial heat in the forty-day voyage.

Members of the steward staff reported with diarrhoea and a temperature of 100° F. (37.8° C.) on the day the ship sailed from Kure, in Japan. As eight men sickened in twenty-four hours it immediately became obvious that an epidemic was threatening and that it was necessary to isolate the cause before the community on board were overwhelmed.

In investigating the outbreak the following factors were taken into consideration. The issue of bread was common to the whole ship and so was water: these items were therefore not suspect. Ruling out bread and water and issued foods as a cause of the enteritis, there was left the handling of the food and the possible contamination of utensils by washing up: washing-up was not thought to be a factor, as the engineer officers were affected as well as the stewards and five of the passengers. Utensils were washed up in three separate places, so a common link was unlikely. This left attention focused on the pantries where cooked food was handled. Of necessity in catering for large numbers, food is often prepared or part served hours beforehand. Some of the staff are of low intelligence and are often antisocial in that it is difficult to educate them in personal cleanliness and hygienic methods of food-handling.

No laboratory investigations were made, as there were no facilities. All cases of enteritis or gastro-enteritis were treated in their own quarters as the ship's hospital was full of other patients, either invalids on passage or more acute cases which had priority. Only one medical orderly was provided for all duties.

Points in Dealing with an Epidemic

Owing to the general lack of appreciation of the results of preventive measures and the impossibility of securing the full co-operation of a large group of men, many of whom are in their present employment because they are misfits in the community ashore, a "blunderbuss" approach may be necessary. This can be achieved by removing the affected catering staff from duty and giving them energetic treatment designed to stop the diarrhoea in a day, combined with the routine measure of standing the men off duty until they say they want to go back to work, thus appealing to the really sick, who are only too thankful for a chance to lie up. At the same time the opportunity of being off duty attracts those who take the attitude that it is "only a touch of diarrhoea" and who would otherwise carry on with their duties to the risk of those they attend. It is essential that all patients should be given a brief talk on elementary personal and food hygiene before they return to duty.

The following points have to be borne in mind in dealing with a food-poisoning epidemic: (1) The ship has to continue its normal voyage and daily routine. (2) As a matter of commercial industrial practice all steps have to be taken to avoid an epidemic among the passengers, because (*a*) many would retire to their cabins and expect to be given individual attention, for which there may be no staff available, (*b*) the ship might run out of essential remedies, and (*c*) there might be a loss of reputation to the shipping company. (3) Lack of co-operation from men of the equivalent of the foreman group who have spent many years at sea: they do not report sick themselves and do not encourage their juniors to do so. Their attitude may be the biggest obstacle to the carrying out of recommendations with any thoroughness.

The foregoing points show how to treat outbreaks of food-poisoning under normal conditions of passenger accommodation. Similar outbreaks are well known in troopships under purely Service conditions, when thousands of troops may be affected simultaneously, usually by an epidemic enteritis suggesting Sonne dysentery.

Diagnosis

The diagnosis of an outbreak of food-poisoning is best considered by the time factor and the symptoms that arise. If the causes are placed in order of time of onset then they can be presented as follows:

(*a*) *Metallic poisoning.*—Cadmium, antimony, and arsenic are possible risks, but poisoning with these substances is not associated with pyrexia. The onset is practically immediate in acute cases, and presents a picture of violent

irritation of the gastro-intestinal tract which can persist over a period of days. In addition cadmium causes a form of bronchitis. Such metallic poisoning may be related to the preparation of citrus drinks in plated or enamelled containers.

(*b*) Staphylococcal or other toxins from the growth of the organism on some article of food contaminated from a septic finger or a boil. The onset is often within an hour and there is an acute gastritis, sometimes with an enteritis. Usually the temperature is not raised, though there are exceptions. This is a single explosive incident unless a food-handler with a lesion on his hands remains undetected to contaminate other foods on another occasion.

(*c*) Infection by *Salmonella* organisms leads to a gastro-enteritis or enteritis with pyrexia; this occurs some hours after the ingestion of the organisms. Frequently an outbreak of salmonellosis occurs as a result of some single meal, but the continued existence of the organisms depends on some reservoir of infection, and this may be animal or human. Infection of animal origin may spread from the intestinal canal of rats and mice or from the oviduct of fowls, especially ducks. In this connexion the use of bulk liquid egg for catering must not be overlooked. Human spread is from the infected bowel by faecal contamination due to lack of elementary hygienic conduct by a food-handler.

(*d*) True dysenteries can run a relatively mild course. They have an incubation period of two to five days and present a gastro-enteritis or, more often, an enteritis which is accompanied by a pyrexia. It is to be noted that the types of dysentery vary in frequency and virulence in different parts of the world. For instance, Sonne dysentery is common in Europe but relatively less common in the Far East. The spread is by faecal contamination from the infected human bowel. The excretor may be symptomless and the excretion intermittent.

(*e*) Typhoid or paratyphoid fever causes a general systemic infection, usually presenting at first as a pyrexia of unknown origin.

Discussion

It would appear that the cases occurring during the outbreak recorded above could have been due to either a variety of *Salmonella* or, most likely, a mild form of dysentery, as the essential features were an enteritis with pyrexia. In view of the persistence of the outbreak the infection must have been from some reservoir of infection, which may well have been a human excretor employed in the handling of the food supplied from the first-class galley. The interesting point is that by standing off duty those food-handlers who were clinically affected it was possible to keep the infection from the group of 250 passengers with only a few exceptions. In the absence of any bacteriological information no other or more accurate explanation of this success can be offered.

In considering the origin of the infection the history is of extreme importance. My cases occurred during a period of weeks. This means that various items of food were infected. It is not possible to think that these several dishes were each carrying an identical infection before handling. The only inference is that they were all infected from some common source during preparation, an interval of a few hours before serving permitting incubation of the organism. This had to be from some reservoir of infection, and under the circumstances this was more likely to be the bowel of a human carrier or case, or alternatively it might have been from the presence of infected mice or rats: in this instance there was no great infestation of the ship with rodents. Salmonella organisms frequently persist in the human bowel for weeks or months after an infection which may have been so slight that it could be forgotten or ignored. Such a carrier state in a food-handler is an inherent risk to any community where mass catering has to be provided. There are no certain tests other than stool examinations, and these may have to be repeated in order to deal with the phenomenon of intermittent excretion if there are no bowel symptoms. These excretors may not infect food if they maintain elementary rules of hygiene and wash their hands after urination or defaecation and on all occasions when re-starting work after being away for any other reason.

A careful history and clinical examination will do much to give a reasonably exact diagnosis based on the factors mentioned above. Examination of the menu will often point to an article of food common to all cases. The staff who prepared it must be followed up and their bowel history reviewed.

The alternative diagnoses of epidemic vomiting and Bornholm disease must not be overlooked. The former is epidemic apyrexial vomiting, either as a single act or repetitive with no other symptoms; the latter displays the typical acute abdominal pain which earned it the alternative name of the "devil's grip." These complaints are of the greatest significance, as they are not food-borne, although they present alarming gastro-intestinal symptoms.

A full bacteriological investigation is difficult owing to the impossibility of having a complete set of equipment always available and a medical officer fully trained and alert to use it to its full advantage. The practice of inexpert and unaccustomed bacteriology is to be deprecated, as false results are worse in every way than no results at all: all that the ship surgeon should do is to use sound judgment in the collection of specimens in appropriate containers under sterile conditions, and to appreciate what are the essential investigations to demand of the laboratory ashore. He must understand the epidemiological aspect of the problem and be able to rationalize his approach. A careful analysis of any outbreak will show clear routes of infection; adequate preventive measures must then be taken. A weak approach leads to confusion, and the subsequent strengthening of precautions can only cause resentment. Strong action can easily be remitted as improved conditions warrant.

It is in dealing with an outbreak such as the one described that the surgeon will really show his administrative skill, although here it must be said that he may be helpless without the full support and collaboration of the captain and other officers, particularly the purser and chief steward. On the one hand, the outbreak must be fully gone into and, on the other, the measures taken must be adequate, relatively simple, and be understood by the staff, who must have induced in them a feeling of personal responsibility in coping with the problem. It causes a glow of respect for some predecessor at sea when an elderly steward confides, reminiscently, "Me and the doctor . . . we fixed it between us!"

It is not possible to comment here on the standards of training in hygiene and epidemiology necessary for those seeking a permanent career at sea in what is one of the most responsible forms of isolated single-handed medical practice. Subject to the overall command of the captain, which at all times must remain unchallenged, it appears to be necessary for the surgeon to have the fullest power to intervene in the conduct of the catering department of the vessel in order to secure appropriate measures for the prevention and control of food-poisoning. Whether this should be done by company regulation or by legislative amendment is immaterial. It is a matter for surprise that the shipping companies do not take more active steps to preserve their reputation in this field.

If the organization of the ship is understood and the places where food is subject to contamination are noted, then it is relatively easy to take steps when an outbreak occurs. The pantries and still-rooms must always be investigated and the previous medical history of the staff recorded. Where there are intestinal symptoms accompanied by pyrexia the infection is by a living organism and a human excretor must always be suspected. A careful and rational approach will indicate the necessary line of action. It is quite possible to deal with the outbreak first and to conduct the laboratory investigation later by preserving specimens by refrigeration.

Summary

The organization of the catering services of a passenger ship is described.

Typical outbreaks of enteritis and gastro-enteritis are mentioned.

Differential diagnoses are discussed with reference to staphylococcal, salmonella, and dysentery infection.

Methods of dealing with an outbreak are outlined.

I wish to acknowledge the encouragement of the chairman and members of the Medical and General Committee of the Association of Sea and Air Port Health Authorities following an address based on a previous article in the *Journal of the Royal Naval Medical Service*. I also had the benefit of the comments of Dr. W. C. Lethem, of the Ministry of Food, Dr. Maurice Williams, medical officer of health, Southampton, and Dr. Morgan, medical officer to the Port of London Health Authority.

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ENTEROCOCCAL ENDOCARDITIS

BY

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In subacute bacterial endocarditis the importance of *Streptococcus viridans* as the causative organism is well recognized. It is not, however, generally appreciated that other bacteria may be involved. Out of 31 cases of streptococcal subacute bacterial endocarditis, Horder (1909) found that eight were due to *Streptococcus faecalis*, and Rantz and Kirby (1943) isolated this organism in 3 out of 16 cases of the disease. However, in large series Sirota *et al.* (1947) and Loewe *et al.* (1951) reported an incidence of the enterococcal variety of 3.2% and 3.8% respectively.

The first case of enterococcal endocarditis was described by MacCallum and Hastings in 1899, the causative organism being the *Micrococcus zymogenes*, now recognized as *Streptococcus zymogenes*. Although several cases have been reported since then, the importance of the enterococci in causing subacute bacterial endocarditis has not been stressed. The following two cases, therefore, are thought worthy of record, constituting only the fifth British report (Andrewes and Horder, 1906; Horder, 1909; Braxton-Hicks, 1912; Cates *et al.*, 1951).

Case 1

First Admission.—A locomotive foreman aged 63 was admitted to hospital on April 30, 1947, with a two-years history of increased frequency of micturition, especially nocturnal, and dysuria without haematuria, culminating in acute retention of urine. His general condition was good. The blood pressure was 165/80, and no abnormalities were recorded in the cardiovascular and respiratory systems. The bladder was distended almost to the umbilicus and the prostate was enlarged, hard, and nodular.

Under general anaesthesia a suprapubic catheterization by the Riches technique was performed, followed by daily bladder lavage. On May 15, under general anaesthesia, a modified Millin prostatectomy was performed; the prostatic capsule was sutured, the bladder was closed with prevesical drainage, and perineal urethrostomy was performed, with subsequent daily lavage. A pyrexia of 100.4° F. (38° C.) on the second post-operative day responded after three days to a full course of sulphadimidine. Convalescence was uneventful apart from a mild thrombophlebitis in the left leg, and he was discharged on June 9. When seen again some weeks later there were no urinary or other symptoms, although he had very slight oedema of the feet and some anaemia (red blood cells, 3,580,000 per c.mm.; Hb, 69%, or 10 g.); the urine contained albumin, and culture produced a growth of coliform organisms.

Second Admission.—On December 10 he was admitted to the medical department, complaining of malaise, loss of weight, and three attacks of sudden onset, consisting of dyspnoea with palpitations, throbbing headaches, and sweating; each passed off after about half an hour. Examination revealed pallor of the face and mucous membranes, with slight cyanosis, slight clubbing of the fingers, dyspnoea on movement, and evidence of loss of weight. The pulse rate was 90 a minute and collapsing in type. The blood pressure was 188/62. There was no clinical enlargement of the heart. Auscultation revealed a high-pitched musical systolic murmur maximal in the aortic area, and, it was thought at this stage, also an early diastolic murmur. There were no other abnormalities. During most of his time in hospital he had an irregular pyrexia of 99–101° F. (37.2–38.3° C.). Subsequently a definite aortic diastolic murmur became clearly audible. The urine contained a dense cloud of albumin and a moderate amount of deposit consisting of 50–100 pus cells, 10–20 red blood cells, and innumerable motile organisms per high-power microscopical field, while culture yielded a heavy growth of coliform organisms. Several unsuccessful attempts were made to overcome the urinary infection, using various combinations of sulphonamide compounds, potassium citrate, and calcium mandelate.

On January 21, 1948, after ten days' aerobic and anaerobic incubation, blood culture revealed a pure growth of a non-haemolytic *Str. faecalis*. Subsequently he received several blood transfusions, but his condition steadily deteriorated with the development of petechial haemorrhages and oedema of the legs and uraemia. Death occurred on February 8.

Necropsy Findings.—The cause of death was congestive cardiac failure. The heart weighed 720 g. and showed gross dilatation of the right auricle and ventricle and hypertrophy of both ventricles, especially in the left. Subepicardial haemorrhages were present at the junction of the superior vena cava with the auricle. Large vegetations were present on both cusps of the mitral valve, forming a protuberant mass on the aortic cusp, which showed aneurysmal bulging into the auricle. There were also vegetations on the three cusps of the aortic valve and on the wall of the aorta just above the left posterior cusp. The aorta showed a moderate degree of atheroma. At the hilum of the left lung there was an organizing thrombus of a vessel, and the lower lobe contained an infarct. The spleen contained a recent infarct of the upper pole. Small haemorrhages were found in the kidneys, throughout the submucosa of the bladder, and in the subarachnoid space on each superior parietal surface of the brain. The other organs revealed no significant changes.

On histological examination the kidneys showed healed glomerular embolization of a few glomeruli; one glomerulus was observed to contain a mass of bacteria.

Cultures from the heart valves and the spleen yielded a growth of *Str. faecalis*.

Case 2

A primigravida aged 25, who had suffered from rheumatic fever at 12 and 17 years, had a forceps delivery on November 18, 1950. Subsequently she was pyrexial, but after receiving penicillin the temperature settled and she went home three weeks later. On December 25 swelling with intermittent pain and restriction of movement began in the fingers of the right hand, gradually spreading up the forearm to the elbow. The condition lasted for about a week, and subsequently all the larger joints were affected by a wandering polyarthritis. Throughout January, 1951, she felt generally unwell and suffered from night sweats, her temperature often being about 101° F. (38.3° C.). About the end of January a blood culture showed *Str. faecalis*, insensitive to penicillin but sensitive to streptomycin, chloramphenicol, and aureomycin. She was treated with chloramphenicol, 4 g. daily for 14 days, and then, because of the nausea and malaise induced, with streptomycin, 2 g. daily for six days. Her temperature rapidly became normal. On February 18 she complained of a severe headache and her temperature was 99.8° F. (37.7° C.). She was admitted on February 19.

On examination pallor of the skin and mucous membranes and clubbing of the fingers were noted. The blood pressure was 110/60; the pulse rate was 72 a minute, collapsing in type. The apex beat was located in the fifth intercostal space, 5¼ in. (14 cm.) from the midline. The cardiac impulse was forcible and heaving. The heart sounds were slapping in character; there were to-and-fro systolic and diastolic murmurs at the aortic area and a rough systolic murmur in all other areas. No other abnormalities were noted.

The blood count showed some anaemia (red cells 3,900,000 per c.mm.; Hb, 68%; white cells, 9,700 per c.mm.). On February 22 blood culture showed a heavy pure growth of *Str. faecalis* sensitive to about 10 units of penicillin, aureomycin, and chloramphenicol per ml., but insensitive to at least 100 units of streptomycin per ml. Treatment had been initiated with chloramphenicol, 3–4 g. daily, but on February 26 this was replaced with penicillin, 6,000,000 units daily, and on the 27th aureomycin, 4.5 g. daily, was added. From March 8 the temperature was normal, and the general condition became much better. The cardiovascular state improved considerably. On March 21 the haemoglobin was 84%. The patient was discharged on March 22, to continue with the penicillin and aureomycin for a further month.

She remained well during this time, but died suddenly, apparently from left ventricular failure, after a period of exertion.

Post-mortem examination of the heart showed hypertrophy and dilatation of the left auricle and ventricle, rheumatic endocarditis of the mitral and aortic valves, and the large fleshy, thrombotic vegetations of subacute bacterial endocarditis on the three aortic valve cusps and on the aortic aspect of the anteromedial cusp of the mitral valve; the vegetations were sterile on culture.

Discussion

For the development of bacterial endocarditis, as pointed out by Hadfield and Garrod (1947), two conditions are necessary: a portal of entry to the blood stream for the organisms, and a susceptible state of the heart valves.

Skinner and Edwards (1942), in their review of 37 proved cases of enterococcal endocarditis from the literature, found that in 14 in which the portal of entry was stated the urinary tract was responsible in two cases (Meyer, 1927; Fuss, 1927), and the genital tract following abortions in three others (Tidow, 1929; Dumas and Josserand, 1933; Wallach, 1934). The two cases of Meyer (1927) and Fuss (1927) had an enterococcal urinary infection, and the endocarditis followed surgical relief of a urethral stricture. Other cases have been reported following urethral manipulation, cystoscopy, or prostatectomy, by Skinner and Edwards (1942), Hein and Berg (1949), Alexander (1950), Cates *et al.* (1951), Loewe *et al.* (1951), Merritt (1951), Robbins and Tompsett (1951), and Finn and Kane (1952)—19 in all. Sirota *et al.* (1947) found in 26 cases of enterococcal endocarditis at the Mount Sinai Hospital that "the source of infection was traceable in 10 cases to recent infection or operative manipulation of the genito-urinary tract, and in one to a septic criminal abortion." Five other post-abortional cases have been reported by Waaler (1937), Harvier and Sarrazin (1948), Robbins and Tompsett (1951), and Cates *et al.* (1951). Leaman *et al.* (1949) observed a case developing one week after a full-term delivery, the organism being isolated from the cervical discharge and from the blood.

In Case 1 the portal of entry undoubtedly was associated with the operative procedures. In Case 2 infection probably occurred through the manipulation and instrumental intervention of the delivery.

It may be noted from the literature that the entry of organisms into the blood stream following urogenital procedures occurred very commonly, yet much less often resulted in bacterial endocarditis. Merritt (1951) found eight cases of endocarditis as a complication of 7,000 transurethral prostate resections, the incidence being 10% in cases known to have had valvular heart disease. This apparently confirms the importance of underlying valvular disease; nevertheless the latter may be modified by the varied characteristics of different bacterial species. Indeed, Rantz and Kirby (1943) reported that enterococcal endocarditis occurred in persons with normal valves more often than other streptococcal infections of the endocardium. They described this in two cases; likewise, Loewe *et al.* (1951), Wallach (1934), and Skinner and Edwards (1942) in four other cases. There was neither a rheumatic history nor clinical evidence of rheumatic heart disease in other cases reported by Guss (1948), Hein and Berg (1949), Dreher (1950), Merritt (1951), Loewe *et al.* (1951), and Finn and Kane (1952)—seven in all. The enterococcal infection in Case 1 was superimposed on normal heart valves.

In general the symptomatology and physical signs in enterococcal endocarditis are similar to those seen in the *Str. viridans* variety. Severe precordial pain may occur. Wallach (1934), Rantz and Kirby (1943), and Loewe *et al.* (1951) have emphasized the frequency of focal suppurative lesions in the myocardium and in the organs peripheral to the heart. In consequence splenic rupture with fatal peritonitis has twice occurred. Foci of suppuration may continually discharge organisms into the blood stream, thus necessitating prolonging the period of treatment. The actual endocarditis lesions are more of the ulcerative undermined type than the exuberant, friable, thrombotic, cauliflower-like masses of the viridans variety (Loewe *et al.*, 1951).

The enterococci are very resistant organisms, although, as regards *in vitro* inhibition of growth, sensitivity is probably greatest to aureomycin. Hunter (1950) has pointed out that sensitivity tests which measure only inhibition of growth may be misleading in regard to effective therapy—a fact borne out in respect of aureomycin (Cates *et al.*, 1951; Finn and Kane, 1952). Cates *et al.* (1951) and others have found that the addition of the bacteriostatic agents chloramphenicol, aureomycin, and terramycin reduces the *in vitro* bactericidal rate of penicillin on enterococci. In reviewing the literature since 1947, comprising 37 reports and involving 86 cases, failure of treatment was found in 46 patients. A combination of penicillin in doses of 6–12 mega units daily and streptomycin, 2 g. daily, was curative in 16 cases (Hunter 1950; Robbins and Tompsett 1951), while large doses of penicillin, over 10 mega units daily, with or without caronamide, about 24 g. daily, to augment blood concentration by inhibition of renal tubular excretion, were effective in eight cases. These two lines of treatment offer undoubted promise; they should be continued for at least six weeks and preferably longer.

Leaman *et al.* (1949) have emphasized that before initiating any treatment complete bacteriological identification and classification of the pathogen are of primary importance. This is especially so in view of the report of Wheeler and Foley (1945) that strains which would have been classified as *Str. viridans* by methods other than group precipitation tests were often found to belong to the Lancefield Group D (to which all of the four recognized species of the enterococcal group belong). Frequent assessment of the changes in sensitivity of the organism is desirable in order that the therapy may be efficiently controlled.

As pointed out by Dreher (1950), the determining factors in the success or failure of treatment are the early administration of adequate amounts of the antibiotic, the resistance of the infecting organism to the antibiotic, the critical nature of embolic phenomena, and the degree of cardiac damage, both valvular and myocardial, which precedes, accompanies, and follows treatment.

Summary

Two cases of enterococcal endocarditis—in a man aged 63 following suprapubic prostatectomy with perineal urethrostomy, and in a woman aged 25 following a forceps delivery—are described.

The importance of the enterococcus in the production of subacute bacterial endocarditis is noted, especially in cases without previous rheumatic heart disease.

The ease of production of bacteriaemia, and the possibility of endocarditis, following genito-urinary infection and manipulations, are emphasized.

The importance of proper bacteriological study of the organisms isolated in endocarditis and the determination of their sensitivity to antibiotics are stressed.

The difficulties of treatment owing to the resistance of the enterococcus are noted. Early, adequate, and prolonged therapy with appropriate antibiotics is advocated.

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Medical Memoranda

Acute Meningo-Encephalitis as a Complication of Glandular Fever

I should like to add the following case to the one I recorded previously (Librach, 1952).

CASE REPORT

An unmarried female fitter aged 19 was admitted as a case of poliomyelitis on July 12, 1952. For five days she had complained of the gradual onset of headache associated with nausea and vomiting. Previous illnesses included measles, pertussis, and chicken-pox. Tonsillectomy had been performed in infancy. She had had no recent or remote inoculations. There was no one else ill at home.

On examination her temperature was 101.6° F. (38.7° C.), pulse rate 84, and respirations 16. She was not acutely ill. Her ears, nose, and throat were normal. A few small neck glands were present. The spleen was not felt. Apart from slight neck stiffness, there were no neurological signs. Treatment included sulphonamides and penicillin for the first 48 hours.

On July 14 the temperature was normal and no meningeal signs were elicited. On July 18 she was pale, and recrudescence of headache and vomiting occurred. There was marked oral foetor and furring of the tongue. Fine lateral nystagmus to the right was seen. On July 20 a normal menstrual period began, associated with continued vomiting and an irregular blotchy erythema of the trunk. Two days later she was quite well. On July 20 minimal gland enlargement affecting the cervical, axillary, and inguinal groups was noted, together with a palpable spleen. On August 2 she was discharged home. When seen again as an outpatient on August 16 she looked well, but felt tired.

Investigations.—July 15 : White-cell count, 7,200 (polymorphs 40%, lymphocytes 44%, monocytes 16%). Glandular fever cells present. Cerebrospinal fluid : 10 ml. slightly opalescent fluid ; cells, 89 per c.mm., all small lymphocytes ; protein, 30 mg. per 100 ml. ; chlorides, 760 mg. per 100 ml. ; sugar normal ; globulin normal ; culture sterile ; no organisms seen on direct examination. Paul–Bunnell tests (blood) ; July 17, 1 in 64 ; July 26, 1 in 128+ ; July 31, 1 in 128+ ; August 18, 1 in 16.

COMMENT

Although no specific signs of glandular fever were present on admission, in the light of previous experience a white-cell count was done ; this showed a characteristic mononucleosis. The Paul–Bunnell test on the blood was at first borderline, but later showed a diagnostic rise in titre to over 1 in 128, remaining at that level for seven days, and then falling quickly to 1 in 16. The maximum titre corresponded with the occurrence of gland and splenic enlargement, but with recovery from the nervous symptoms.

In contradistinction to the previous case, the cerebrospinal fluid was abnormal and showed 89 lymphocytes per c.mm. three weeks after the first complaint of headache, and when the neurological signs had gone, minimal gland and splenic enlargement occurred—that is, the lymphadenopathy *followed* the nervous signs.

The neurological manifestations have been reviewed briefly by Tidy (1952). He stresses the importance of the timing of the Paul–Bunnell test, which may be occasionally positive in the cerebrospinal fluid. It will be recalled that the present patient was admitted as a possible non-paralytic poliomyelitis case. It would seem eminently worth while to do routine white-cell counts and Paul–Bunnell tests in these cases, for in this way more might be learnt about the behaviour of this strange malady, and its true incidence appreciated. The relation, too, of the heterophil antibody titre to the stage and severity of the illness would also prove of value, especially if tested for both in blood and cerebrospinal fluid simultaneously, for detailed information regarding both in relation to one another and to the illness is lacking.

Clinically the most striking feature, apart from the bizarre nature of the symptoms, is the rapidity with which a structure that appears to be seriously affected recovers, and this is especially so in the neurological complications. Recovery, too, is usually complete and permanent, and without residual defects or deformities. Death is an uncommon termination of glandular fever, but in the absence of an extensive literature on the neurological complications it is difficult, if not impossible, to dogmatize on the prognosis. Generally speaking, it can be said to be excellent.

There have been few reports in the literature of the pathological findings in fatal cases with C.N.S. involvement. Dolgopol and Husson (1949) describe in detail such a case which occurred in a young white woman, aged 19, whose main symptoms were diplopia and dysphagia. Macroscopically, the brain was moderately congested, the meninges equally so, but the grey matter of the cord was diffusely haemorrhagic. Microscopically, the most important features in the brain were severe degenerative changes in the nuclei of the third and fourth cranial nerves and in the ventral portion of the inferior reticular nuclei just above the inferior olives. The spinal cord showed extensive recent perivascular haemorrhages limited to the posterior horns in the upper cord but also present in the anterior horns and white matter in the lumbar segment, where some demyelination was also present.

Thomsen and Vimtrup (1939) also described six fatal cases complicated by central respiratory paralysis, one of which showed similar degenerative changes in the medulla.

In view of the current interest in bulbar poliomyelitis it might be as well to consider in differential diagnosis the bulbar involvement which occurs in glandular fever, and to perform routine Paul–Bunnell tests in such cases.

I thank Dr. E. Dunnett and Dr. M. Rogers for their help in treating this case; Dr. R. Tannahill, consultant in infectious diseases, for helpful criticism and for permission to publish; and Mr. L. Whittaker for the laboratory findings.

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Agranulocytosis Caused by Cinchophen

Agranulocytosis caused by cinchophen ("atophan") is very uncommon. Cushny (1947) does not list agranulocytosis amongst its toxic effects. Dameshek (1944) finds it a rare cause. Plum (1937) mentions only Shapiro and Lehman's (1936) case. Fitz-Hugh and Comroe (1933) report a case due to *ortho*-iodoxybenzoate, which contains cinchophen. Coventry (1939) mentions a further case. Rawls (1944) quotes a case due to vitamin K, but cinchophen was also taken, and was probably responsible. In view of the rarity of the condition the following case is reported.

CASE REPORT

A company director aged 56 complained of a painful left nostril on July 9, 1951. Two days later he felt hot and cold, with discomfort in his throat. His temperature rose to 102° F. (38.9° C.) with profuse sweating. The third day his nose became red, his throat sore, and swallowing difficult. His anal region became painful and a red area appeared over his eyebrow and cheek. Anorexia, constipation, and general malaise were present. On July 13 his sore throat, dysphagia, and sweating became worse and a swelling appeared under his jaw.

Next day he looked ill, and his temperature was 101° F. (38.3° C.), pulse 66, respirations 18. Exudate was present over the tonsils, but no ulceration in the mouth. Under the left side of his jaw was a large tender swelling. His left nostril showed a necrotic area and the anus extremely tender ulceration. The liver and spleen were not palpable and there were no petechiae or jaundice. The heart, lungs, and central nervous system were normal. No other lymph nodes were palpable. A clinical diagnosis of agranulocytosis was made, being confirmed on July 16 by blood examination showing a white-cell count of 400 with 2% polymorphs (Dr. A. E. Brewer).

For the first few days of the illness he was treated symptomatically with aspirin, "veganin," and "agarol." Penicillin, 1,200,000 units daily, was started on July 14, when agranulocytosis was considered likely, and increased on confirmation on July 16 to 2,000,000 units twice daily together with aureomycin, 1 g. four-hourly, and pyridoxine, 100 mg. intravenously twice daily. On July 17 blood examination showed: white cells, 800 (2% polymorphs, 89% lymphocytes, 4% monocytes, 4% eosinophils, 1% basophils); Hb, 78%; red cells, 4,430,000; C.I., 0.9; M.C.V., 82 μ^3; M.C.H.C., 31%; corrected sedimentation rate (Wintrobe), 39 mm. in one hour. On July 19 the white cells rose to 3,000 (22% polymorphs) and on July 21 to 6,500 (50% polymorphs). On July 26 the treatment was stopped, 32,000,000 units of penicillin and 34 g. of aureomycin having been given. Blood examination on July 28 showed: white cells, 6,200 (68% polymorphs, 30% lymphocytes, 2% monocytes); Hb, 91%; red cells, 5,100,000; corrected sedimentation rate (Wintrobe), 12 mm. in one hour; total plasma proteins, 7.2 g. %. Throughout the treatment vitamin-B complex was given together with hydrogen peroxide mouth washes. The anus was treated with amethocaine hydrochloride ointment. The temperature settled by lysis in three days, remaining normal after July 20. Further recovery was uneventful.

The drugs the patient consumed were investigated. It was discovered that on June 27 (12 days before his illness) he took cinchophen, 7½ gr. (0.5 g.) three times a day for three days, for a painful neck, and he repeated this course twice with three days between each course. The first symptom (painful nostril) appeared at the beginning of the third course (July 9) and after July 11 no further cinchophen was taken. He had also taken "anadin," which contains phenacetin, 2 gr. (0.13 g.), acetylsalicylic acid, 4 gr. (0.26 g.), caffeine, ¼ gr. (32 mg.), quinine sulphate, 1/12 gr. (5.4 mg.); "theogardenal" (phenobarbitone, ¼ gr. (32 mg.), theobromine, 5 gr. (0.32 g.)); "halmagon," which contains magnesium chloride (0.395 g.), magnesium bromide (0.0133 g.), magnesium iodide (0.000067 g.), magnesium fluoride (0.0006 g.), and occasionally vegetable laxatives. The anadin was started in March, 1951, three or four tablets a week, for rheumatic pains. The last tablet was taken on June 26—that is, on the day he commenced cinchophen. The theogardenal was taken intermittently during the previous six months, half a tablet two or three times a day, until he commenced cinchophen. He took halmagon for several weeks for increased frequency till two weeks before his illness. He had also taken cinchophen a year before for a few days without mishap.

COMMENT

The agranulocytosis in this case was thought to be due to cinchophen. It is necessary to consider whether the other drugs could have caused it. Anadin contains aspirin, phenacetin, caffeine, and quinine. No authentic case of agranulocytosis due to aspirin has been traced in the literature. The case reported by Hawkinson and Kerr (1943) is a doubtful one. The two cases reported by Groen and Gelderman (1934) took other drugs as well. Phenacetin has been incriminated as causing agranulocytosis by Kracke (1931) and Kracke and Parker (1934), but Dameshek (1944) considers it doubtful. No case due to caffeine has been discovered.

Agranulocytosis due to quinine has been reported (Corelli, 1934; Vitug, Chavez, and Austria, 1935; Dassen and Fongi, 1935; Faiguenbaum and Gasic, 1938; Franks and Davis, 1943; Efrati, 1943). In Norris's (1936) case amidopyrine was taken as well, and Groen and Gelderman's (1934) two patients consumed other drugs besides quinine. The quantity of quinine in anadin is, however, too small (1/12 gr.—5.4 mg.) to be significant.

As regards theogardenal, agranulocytosis following barbituric acid preparations has been reported (Watkins, 1933, 17 cases; Hadler, 1940; Black and Stanbury, 1947). Clear-cut proof, however, has rarely been obtained, and Kracke (1934) and Dameshek (1944) doubt if the barbiturates have any connexion with it. None of the mineral salts in halmagon have been known to cause agranulocytosis.

Thus cinchophen is regarded as the cause. Proof by eliciting a haematological and clinical response following a test dose by mouth (Plum, 1937) or intradermally was not carried out because of the risk in either case of precipitating an acute attack of agranulocytosis (Whitby and Britton, 1950) and because the intradermal tests are usually negative (Dameshek and Colmes, 1936; Holten, 1937).

From the theoretical aspect cinchophen is phenylquinoline-carboxylic acid, and under certain conditions may liberate free benzene or nitrophenols. Compounds containing either of these induce toxic degeneration of the liver or a paralysing effect upon leucopoiesis, as in the case of arsphenamine, amidopyrine, and dinitrophenol poisoning (Shapiro and Lehman, 1936).

Coventry (1939) reported the case of a man aged 63 who took cinchophen and "anazin" for joint pains, the latter drug containing the same constituents as anadin. Skin tests and test-dose administration were not carried out.

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Familial Paget's Disease of Bone

It is not generally realized that Paget's disease of bone may be familial, although this fact is mentioned in most reviews of the subject. There are at least 77 instances in the literature in which more than one member of a family suffers from this disease, and in over one-third of these more than one generation is involved. Dickson *et al.* (1945) reported the presence of the disease in six relatives, four generations being affected, and also in identical twins of another family. Paget's disease of bone in identical twins has also been noted by Martin (1947) and by Aschner and her colleagues (1952), although the diagnosis in one of the latter twins is very uncertain. Families with four members affected have been described on three occasions (van Bogaert, 1933; Hanke, 1935; Gutman and Kasabach, 1936), and with three members affected, 14 times. The family reported by Camurati (1922) and sometimes quoted in this context does not appear in fact to have suffered from Paget's disease.

A patient with Paget's disease recently treated in this hospital was found to have two brothers and two sisters who had the same condition. The case histories of 51 other patients with osteitis deformans who were treated in this hospital in the five years 1947–51 were then reviewed; a family history of the disease had been noted in three instances; in one case two relatives and in the other two cases one relative had also been afflicted by the condition.

First Family

Case 1.—Mr. F. R. died recently at the age of 76. He had spent the previous few years in hospital and was enfeebled by most extensive osteitis deformans.

Case 2.—Mrs. A. S., sister of Mr. F. R., died at the age of 63. Bowing of her legs was apparent at the age of 51, and a clinical diagnosis of Paget's disease was confirmed by radiography at the age of 56.

Case 3.—Mr. E. R., brother of Mr. F. R., aged 71, is in part-time employment as a labourer and is free of symptoms. His right tibia is somewhat bowed and has an irregular anterior border; a radiograph of this bone showed thickening of the cortex on the anterior aspect, the changes being suggestive of early Paget's disease. This man's serum alkaline phosphatase was slightly raised at 15 King-Armstrong units.

Case 4.—Mrs. A. T., sister of the above, aged 69, first noticed bowing of her legs over twelve years ago. She has advanced Paget's disease with involvement of the skull, spine, thoracic cage, and left leg; recently a sixth cranial nerve palsy has developed.

Case 5.—Mrs. R. T., sister of the above, aged 67, has been a patient in a ward for the chronic sick for over three years. She has extensive advanced Paget's disease and can walk only with assistance.

The only other sibling, a sister, died at the age of 64 and did not, so far as is known, suffer from this condition; the parents were not blood relations, and from the descriptions given by their children they do not appear to have shown any of the obvious deformities produced by Paget's disease, nor was this disease mentioned on their death certificates. Thirteen members of the third generation of this family, with ages ranging from 30 to 58, have been contacted and do not complain of any deformity; the three other members of this generation cannot be traced.

Second Family

Case 1.—Mrs. M. R. began to develop the typical deformities of the legs and head at the age of 50. She later developed deafness and blindness, the latter being due to macular and peripapillary choroidal sclerosis, and finally died at the age of 68 with extensive Paget's disease.

Case 2.—Mrs. J. K., the elder sister of Case 1, also showed deformities at about the age of 50, and also developed deafness and blindness before her death.

Case 3.—Mrs. C. H., the youngest sister of the family, noticed a painful swelling of the right tibia at the age of 46 following a minor injury. Four year later, swelling and discomfort having recurred, a diagnosis of localized Paget's disease of the tibia was made. Recently at the age of 55 the right lower leg showed the typical anterior bowing with an increase in the temperature of the overlying skin. Radiographs confirmed the presence of Paget's disease in the tibia and demonstrated early changes of the disease in the pelvis and one lumbar vertebra. The serum alkaline phosphatase was 41 K.-A. units.

Three other siblings died at the age of 30 or less, one died of carcinoma at the age of 49, and the eighth, a sister, now aged 58, is free of any sign of the disease, as are eight children of the affected sisters, with ages from 25 to 50.

Third and Fourth Families

A man aged 64 developed aching of the legs and lower back at the age of 59 and was found to have osteitis deformans of the skull, pelvis, left femur, and lumbar vertebrae. An elder sister died of Paget's disease at the age of 66.

A man aged 71 with typical advanced generalized Paget's disease reported that his father had bow legs for a few years before his death at the age of 80.

Incidence of Familial Paget's Disease

Dickson and his colleagues (1945) found a family history of the disease in 16 out of 366 cases (4.4%), Gutman and Kasabach (1936) in 4 out of 115 (3.5%), and Locke (1943) in 10 out of 48 cases (20.8%). Da Costa *et al.* (1915), reviewing all cases of Paget's disease reported up to that time, noted a familial incidence in 7%.

The incidence in the present series is 4 out of 52—that is, 7.7%. From the notes of many of the patients it would seem unlikely that any close inquiries into the family histories had been made, and it is possible that a higher incidence of familial Paget's disease might have been found. The other fact which makes it difficult to estimate the true incidence is that many cases are symptomless (up to 27% of some recent large series), the diagnosis being made only when radiographs are taken for the investigation of other complaints.

There can be little doubt that this familial incidence is not coincidental; Montagu (1949) has suggested that the predisposition to the disease may be transmitted as an incompletely dominant gene carried on an X-chromosome.

My thanks for permission to publish details concerning patients who had been under their care are due to Professor Sir James Paterson Ross, Dr. Bertram Jones, Dr. K. Kropac, Mr. I. G. Williams, and Dr. A. W. Spence, who also gave helpful advice.

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Reviews

HAZARDS OF IMMORTALITY

An Unsolved Problem of Biology. By P. B. Medawar. University College, London, Inaugural Lecture. (Pp. 24; illustrated. 5s. net.) London: H. K. Lewis and Co. 1953.

Why do living creatures die? Part of the answer is clearly that they are constantly exposed to the fatal hazards of injury and infection. Wild animals rarely survive for long the naked cruelties of Nature. Only when shielded in captivity do they live on to show senescence. Man follows this general pattern. Two thousand years ago death was likely to overtake him before he reached his fourth decade; with the passage of the centuries his life expectancy slightly increased. But it is only in the past 60 years that the outlook has reached the prophet's span of three-score years and ten. With this increased longevity has come a marked change in the demographic pattern of the population and also a change in the causes of death. Infections no longer exact their earlier toll; cardiovascular disease and cancer now take their places as Captains of the Men of Death.

But this leads to another question. What would happen if all external hazards could be eliminated? Would the organism be immortal, or is there an inevitable limit to its life span determined by inherent factors—a property which Gowers in the clinical field had named "biotrophy"? In a sense the protozoon reproducing by fission may be immortal and, in the same sense also, the germ cells of higher organisms. But what of the organism as a whole and its intrinsic units? The problem is of course complicated, but the "holism" of the organism, on which continuation of life depends, is based upon the symbiosis of a society of cells. The isolated chicken's heart, for instance, may be made to survive for extraordinary periods.

This problem is the core of Professor Medawar's unsolved problem of biology. He uses the term "ageing" to indicate simply the passage of time; when he wishes to indicate those changes, both structural and functional, which ageing colloquially signifies, he uses the word "senescence." He discusses briefly the measurement of senescence, and shows that, when assessed in the individual by such tests as wound healing, hearing acuity, physical strength, endurance, and the accuracy of muscular co-ordination, several different answers must be given.

Taking vulnerability to the mortal hazards of life as a measurement of vitality, it is simple statistically to construct a curve which measures the likelihood of dying within a selected age period, and from such a curve to compute the death rate at any age, the mean expectation of life at any age, and the likelihood of one age living to another. Any such curve, however, represents both (*a*) "the accumulated sum of the effects of recurrent stress or injury or infection," and (*b*) "the innate or ingrained senescence"; and to dissociate these is practically impossible. Professor Medawar is chiefly concerned with innate senescence, and to illuminate his theme he makes fascinating use of a model of test-tubes with a breakage rate of 10% per month, in which the breakages are made good by replacements mixed randomly with the pre-existing stock (analogous to reproduction). He is able to dispel two commonly held but mistaken views: the first is that a potentially immortal population, subject to the hazards of Nature, will be "numerically overwhelmed with dotards"; and the second, that senescence in higher animals is a consequence of their having a post-reproductive period of life—in fact, this post-reproductive period results from senescence. If after a certain age the test-tubes disintegrate (that is, are mortal), the consequences to the postulated race of test-tubes will depend upon the age at which dissolution occurs. Moreover, he shows that the force of natural selection weakens with increasing age, and that if a genetic abnormality appears late enough in life its consequences may be completely negligible; thus the postponement of the time of overt action of a noxious genetic factor is equivalent to its elimination.

Other consequences, including clinical problems of heredity, are touched upon in this necessarily brief but most stimulating lecture. It should be read by all who are interested not only in the problem of senescence but also in the use of mechanical models, despite their manifest limitations, in the elucidation of biological problems. For Professor Medawar the origin and evolution of senescence are not insoluble genetical mysteries, but the theory he offers is, as he frankly recognizes, hardly self-sufficient. We may, however, look with confidence to Professor Medawar to bridge many of the existing gaps in our knowledge of this important topic.

HENRY COHEN.

STARVATION AT LARGE

The Limits of the Earth. By Fairfield Osborn. (Pp. 175. 12s. 6d.) London: Faber and Faber, Ltd. 1954.

Sociologists and nutritionists are agreed that the inadequate production and defective distribution of food are already causing chronic malnutrition in large sections of the world's population. Thus in many parts of Asia and Africa life is passed in a state of partial starvation, with the threat of acute famine never far away. In spite of these privations, however, the world's population is rising rapidly, particularly in those areas where food is already scarce. Few will deny the possibility that starvation eventually may spread from Bengal and Central Africa to London and New York, but opinions differ about the steps which should be taken to avoid this danger. Some agricultural authorities believe that salvation lies in the direction of more intensive and efficient farming. Backward populations will become less prolific when they are better fed, and have an economic status which will divert their interests from procreation to the purchase of luxuries. Others consider that one of the main factors causing the increase in the world's population is the suppression of disease by the progress of medical science. It is therefore the duty of medical science to provide some form of birth control cheap and simple enough to be used by uneducated and improvident populations.

Mr. Fairfield Osborn considers that time is too short for such arguments, and that action should be taken at once both to increase food supplies and to limit births. His interesting, instructive, and well-balanced book tells how faulty methods of cultivation have already spoilt large tracts of the earth, how further depredations may be avoided, and how new areas may be brought into cultivation. Soil erosion, he points out, was no novelty in the time of Plato, who bemoaned the derelict state of the land in Attica. Sometimes conditions of land ownership are another hindrance to production; in the Amazon basin the development of vast inland areas may be held up by the owners of property on the banks of the river system. As an American he emphasizes that shipping facilities would be quite inadequate to give effect to the idea of feeding India with surplus food from his own country. In a chapter on "Horizons and Mirages," he discusses unusual or untried sources of foods, such as fish grown in ponds, yeasts, sea weeds, marine plankton, and artificially cultivated *Chlorella.* But in the end he questions whether the purpose of civilization is simply to find how many human beings can be crowded on to the earth, and whether the quality of the world's population is not even more important than its quantity.

T. MOORE.

MICROBIC ADAPTATION

Adaptation in Micro-Organisms. The Third Symposium of the Society for General Microbiology held at the Royal Institution, London, April, 1953. Edited by E. F. Gale and R. Davies. (Pp. 339. 30s.) London: Cambridge University Press. 1953.

The Society for General Microbiology has again had the enterprise to publish the proceedings of one of its meetings in book form. At the symposium on "Adaptation in Micro-organisms" held in London on April 14–15, 1953,

the 15 papers were already available in print and were taken as read, the meeting itself being given entirely to discussion of them. The present volume contains these papers and what is described as "a somewhat idealized account of the discussion": this is incomplete and condensed, but gives an impression of spontaneity and amplifies the treatment of some subjects in a valuable way. There were eight contributors from abroad, four from the United States and four from Paris. Some of the contributions deal with subjects of direct medical interest, particularly the development of drug resistance; and in this connexion the rival claims of mutation and adaptation as explanations of this change are extensively debated. Others are products of a study of the physiology of bacteria which has progressed rapidly in recent years, devised a language of its own, and attained depths to which exponents of applied branches of the science find it difficult to follow. In this development the fact that bacteria reproduce far more rapidly than any other living things has had a major influence: they are thus convenient objects of study to the biochemist and the geneticist. This volume, as much as any other single publication which has appeared for some time, reflects the advances in fundamental knowledge which have accrued from work of this kind, and the Society for General Microbiology deserves to be congratulated on its production.

L. P. GARROD.

HYPERSPLENISM

Les Hypersplénies. Rapports Présentés au XXIXe Congrès Français de Médecine, Paris, 1953. (Pp. 160. 950 fr.) Paris: Masson et Cie. 1953.

This monograph on hypersplenism is a collection of papers presented at the XXIXth French Congress of Medicine in Paris in 1953. The papers resemble French theses in being reviews of the literature rather than accounts of the work of individuals. The special value of the book to English-speaking readers is the access it provides to the Continental literature in general and the French in particular. Although it is entitled hypersplenism and that subject is fully discussed, the book is by no means limited to that topic. There are sections dealing with the metabolic activity of the spleen, the role of the spleen in iron metabolism, the relation of the spleen to the endocrine system, and the possibility of the manufacture of specific factors such as thrombocytopen. The various lipoid reticuloses are reviewed, and there is an up-to-date account of the diagnosis and treatment of portal hypertension.

The book finishes with a long article on the present conception of Banti's disease by Rietti of Ferrara. This defends the thesis that there are a number of cases of cirrhosis in which the morbid process begins in the spleen, later spreading to the liver, and that the disease can be arrested by removal of the spleen. This is certainly what Banti had in mind, but modern studies, which are based on liver biopsy, measurement of liver function, determination of portal venous pressure and demonstration of anastomoses by venography, suggest that if such a sequence occurs at all it must be indeed rare, and therefore splenectomy is to be discouraged in the treatment of hepatic cirrhosis or oesophageal varices.

L. J. WITTS.

SALMONELLAE AND SHIGELLAE

Salmonellae and Shigellae: Laboratory Diagnosis Correlated with Clinical Manifestations and Epidemiology. By Alfred J. Weil, M.D., and Ivan Saphra, M.D. (Pp. 252; 29 illustrations. 56s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications, Ltd. 1953.

The authors state that "the aim of this book is to make conveniently accessible the factual information needed for the handling of the laboratory aspects of salmonella and shigella infections." The facts may be there but their presentation is such that the reader tends to lose sight of them, either in irritation at having himself to connect disjointed pronouns, sentences, and tables, or in astonishment at the curious phraseology and sudden lapses into colloquialisms. "Outspoken" used to described motility, agglutination, and sedimentation, "stabile" for stable, and "alkaline" for alkali are but a few examples.

Certain figures are separated by several pages, from their keys, and there is some lack of correlation between the numbering of figures and their quotation in legend and text. Again, the dust cover states that there are 252 pages, and 29 illustrations, but the reviewer found 247 pages and, at the maximum, 17 illustrations—the authors themselves listing only 15. There are several spelling inconsistencies. All these are points minor enough in themselves probably, but when multiplied throughout the book make for neither clarity nor pleasurable reading in spite of good paper and large print.

There is much repetition of simple facts in different chapters and tables, whereas more difficult aspects of the subject —for example, serology—are discussed relatively superficially, leading to disproportionate emphasis. The summary of the complex cross-reactions of the Flexner subgroup of *Shigella* in a table with redundant serial numbering and ambiguous terminology confuses the subject further. The controversial classification and nomenclature of the *Shigella* published by Weil, Black, and Farsetta in 1944 is used, though a table of synonyms (with misquotations) is given, and there are no references after 1951. The authors have not quite achieved their prime object in writing this book —namely, to aid in routine diagnostic work.

K. P. CARPENTER.

TRACING THE HEART BEAT

The Heart Beat: Graphic Methods in the Study of the Cardiac Patient. By Aldo A. Luisada, M.D. (Pp. 528; 311 illustrations. 84s.) London: H. K. Lewis and Company Ltd. 1953.

The author of this book gives an account of the various graphic methods which have been applied in the last 50 years to the study of the beat of the heart. There is an historical outline which goes back to the days of Marey, with his plethysmograph and his sphygmograph. As the author points out, these technical matters aim at explaining and completing the data which our unaided senses provide. Our vision is amplified by fluoroscopy; the orthodiagram, the cardiogram, and the sphygmogram extend our sense of touch, as does the phonocardiogram our sense of hearing; and still we have the electrocardiogram, the kymogram, and the ballistogram, which open up an entirely different field. The data these supply have to be fitted into those given by our senses.

The work is very well done. The various techniques and tracings are amply described and the illustrations are clear; the arrangement of the book is excellent. An interesting chapter is the one on the way in which drugs and the like may modify graphic data. In the latter part of the book the author describes the various clinical applications of the graphic methods, giving indications for their use, and the reader learns what may be expected of them. It is really a triumph that he has managed to compress so much information into such a small space. Perhaps at times it is almost too short; for instance, the section on vector cardiograms is condensed into two pages and three figures; the discussion of the cardiac gradient takes little more than a page and almost all the information is conveyed remarkably clearly in the first two-thirds; the last third is less clear. The electrocardiogram is discussed in about 30 pages with considerable success.

The reader might think perhaps that with all these methods there is really nothing that can escape him; yet we know that all machines can lie and not infrequently do. The book might have been even more useful if more had been said about the fallacies which may underlie some of these procedures; but we must give credit to the author for not being too enthusiastic, even about those methods in which he is particularly interested. This is a book well worth reading, and especially so for anyone contemplating the study of one of the subjects described in it. All the initial facts are here and there is an up-to-date list of references at the end of each section. But the name of Mackenzie should surely have been spelled correctly.

TERENCE EAST.

BRITISH MEDICAL JOURNAL
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THE END OF RATIONING

The men who devise the food policy of a nation in times of scarcity do not often hear acclaiming trumpets, though it is true that the crowd bent the knee to Joseph when, after deciding the food policy of ancient Egypt, he rode in the second chariot. But without these men war could hardly be won, and if it were won famine would soon take what war had spared. The end of rationing this week seems to be suitable for a grateful farewell.

Food control began, of course, as a measure to meet wartime scarcity. It was the supply situation which determined, in January, 1940, the first foods to be rationed—butter, bacon, and sugar, and, later on, meat, cooking fat, cheese and preserves—but it developed into a social service, aided thereto by the relatively new science of nutrition. In the result, so far from the health of the population deteriorating during the war, it actually improved. An increase in minor ailments, such as slight forms of peripheral neuritis, was sometimes ascribed to dietetic deficiencies, but expectant mothers and children were more healthy than before, which means that a healthier generation is now maturing. In the last complete year of the war infant and maternal mortality rates and stillbirth rates reached record low levels.

The years following the end of a great war have often been more hungry than the war years themselves: there was, for instance, severe distress in this country, especially of the rural poor, after the end of the Napoleonic campaigns. At the Hot Springs Conference in 1943 some such situation was envisaged. The Ministry of Food was apprehensive of a shortage of energy-giving foods after the war. Indeed, a crisis in world grain supplies did occur in 1946–7, and in this country the rationing of bread and flour came about in 1946. Until then bread had not been rationed, even in the worst crises of war, but shipping space had been saved—and incidentally nutritional advantage had been gained—by raising the extraction rate of flour from 70% to 85%.[1] Rationing of bread was a serious step to take, yet according to the vital statistics the restriction on bread, and later a certain rationing of potatoes, did no harm to the nation's health.

During the war years the civilian supplies *per capita* of some of the principal foodstuffs were actually greater than in the pre-war period. This was true in 1944 of some dairy foods, potatoes, vegetables, and grain products. Even the supplies of meat were only about 11% less *per capita* than before the war. For this happy state of affairs Britain owed much to the Dominions and the U.S.A., to countless individuals in them as well as to their governments. The larger deprivations were in sugars and fats, and perhaps the most noticeable was in imported fruits. Rationing was based on the principle that all essential foods should be equally available to every citizen to the extent necessary to maintain health, and at controlled prices. When rationing came it proved to be more acceptable than had been feared. Probably the period will be remembered, not because of any nutritional inadequacy, but because of inconveniences—queues and ration books—and the disappearance of many dietetic luxuries and variants. Improvements were made in the popular diet for which nutritionists had been pressing for years. This was a great achievement in the face of enemy submarine activity, withdrawal of labour for military purposes, and frequent disorganization of production and distribution. The table was far from being as inviting to the palate as usual, and much was added to the housewife's cares, but from the point of view of availability of health-giving foods the position was even better than before. Control was also extended to the quality of food, the fortification of certain foods (chalk was added to flour and vitamins A and D to margarine), and the use of preservatives.

Criticisms were inevitable over a matter which penetrated into every kitchen, and from a medical point of view many of them appeared in the correspondence columns of this *Journal* and occasionally in the leading articles as well. But, taking it all round, it was a great achievement. A rationing system was devised which was rigid enough to meet the emergency and flexible enough to allow for priorities—for expectant and nursing mothers, for schoolchildren, for adolescents in factories, for certain workers in heavy industrial employment. Provision was also made for special rations for invalids, and for concessions to vegetarians and those whose religion contained some dietary injunctions. During the times of heavy bombing efforts were made to provide in the large shelters

[1] Reduced to 82.5% in 1944 and 80% in 1945, and temporarily raised again to as high as 90% in 1946.
[2] The first Minister was Mr. W. S. Morrison, now Speaker of the House of Commons.

the sort of food which, so far as possible, would help to safeguard the health of the families which were living in such adverse conditions. In addition to the national rationing, much interfamily readjustment was possible, whereby children received more than their scheduled amount of such foods as eggs, jam, and sugar; and adults, after bread-rationing, benefited from the relatively large bread allowance for children. A "points" system, introduced in 1941, eased the situation, as did food parcels from overseas, the establishment of "British Restaurants" and works canteens providing substantial meals at cost price, and the practice, which has remained to some extent as a social habit, of eating out. This last was nothing new in rationing. In the siege of Paris in 1870 newspaper correspondents were remarking that "you have to dine at a restaurant until your ration day comes round again."

For the success of British rationing tributes are due in many quarters. The Ministry of Food, although actually set up in the first week of the war, was not a hastily contrived expedient. A Food Defence Plans Department was in existence in 1936. There was also the precedent of the Ministry of Food of 1916–19, with Lord Rhondda, the author of the system of compulsory food rationing, as its chief figure. The second world war found its "Rhondda" in Lord Woolton, Minister from the early part of 1940 until 1943,[2] who brought to his task great business capacity, persuasiveness (for, even during compulsory rationing, propaganda by persuasion goes quite a long way), and ability to choose the right men. Lord Horder at the outbreak of war was asked to advise the Ministry of Food on the general aspects of wartime feeding, and worked with the Government in that capacity for six years. Another great (and still mourned) figure was the late Sir Jack Drummond, chief scientific adviser to the Ministry until 1946, whose nutritional wisdom, acquired long before the war, laid the British nation under a debt.

Committees must share with individuals the praise that is due. In 1940 a War Cabinet Committee on Food Policy was set up by the Lord Privy Seal, principally to advise on the minimal diet required to maintain health and efficiency under war conditions. It included experts in nutrition, agriculture, and economics. Soon it became evident to that body that numerous questions affecting health were likely to arise in the technical application of food policy, and the Ministry of Health was made responsible for advising the Government on these matters. A standing interdepartmental committee was established, with the Chief Medical Officer of the Ministry of Health (Sir Wilson Jameson) as its chairman.

The Medical Research Council sponsored much of the basic research which went to the support of the scientific side of food policy. The first of two advisory committees on nutrition, having wartime exigencies in view, was appointed by the Council eight years before war broke out. It will be remembered that under the Council's auspices four volunteers, in advance of compulsory rationing, submitted themselves to a diet more severely restricted than any that the civilian population might be expected to have to tolerate, and after three months of exacting tests proved perfectly fit. In 1940, at the request of the Ministries, the Council set up a Food Rationing (Special Diets) Advisory Committee, of which Sir Edward Mellanby was chairman until 1949, and afterwards Sir Harold Himsworth. Its task of prescribing food allowances for sufferers from certain diseases, and determining allocations to invalids recommended by their doctors, was often distasteful, but it was well done, and with derationing this committee is now discharged with honours.

Altogether it has been a hectic but creditable chapter of British history. A population comes out of it with health unimpaired, and perhaps with better food habits, having learned something of food values of which it had known little before, and that efficiency in labour and joy in living are not necessarily imperilled by a tightened belt.

DIETARY CHOLINE AND CARDIOVASCULAR DISEASE

The possible importance of food in the pathogenesis of chronic degenerative diseases of the heart and arteries has recently received some attention. An important paper from Professor Charles H. Best's laboratory in Toronto, which appears in the opening pages of the *Journal* this week, reminds us once more that a dietary deficiency of choline may be of some significance. The investigations leading up to the present series of observations have been going on in Toronto for 30 years, and their development provides an interesting example of how important discoveries may be made by pursuing the reasons for an anomalous finding in experiments designed for a totally different purpose.

When in 1922 Banting, Best, and Macleod[1] announced the discovery of insulin it was at first supposed that an animal deprived of its pancreas could be maintained in health indefinitely by insulin treatment. Two years later it was clear that the position was not so simple. Fisher[2] noticed that depancreatized dogs receiving insulin survived for very

variable periods, those which lived longest showing evidence of pancreatic tissue regeneration. Almost simultaneously Allan, Bowie, Macleod, and Robinson[3] reported that four depancreatized dogs which had died despite adequate insulin treatment all showed gross fatty changes in their livers. This observation was followed up, and by 1930 Hershey[4] was able to report that, while depancreatized dogs seldom survived more than eleven months on a diet of lean meat and sugar supplemented by insulin injections, they lived much longer if either raw pancreas or crude lecithin from egg-yolk was added to their food. The same effect was found by Best, Hershey, and Huntsman,[5] using purified lecithin. From this it was a logical step to find out whether the chemical constituents of the lecithin molecule were effective. In 1932 Best and Huntsman[6] showed that, while sodium oleate and glycerophosphate were inactive, choline was as active as the lecithin from which it was derived. Further work brought to light a wide range of substances, notably methionine, which had a similar action.

So far the hepatic changes only had been studied, and it was not until 1939 that Griffith and Wade[7] pointed out that haemorrhagic lesions of the kidneys also occurred in choline deficiency. In 1952 Hartroft, Ridout, Sellers, and Best[8] announced that with a slightly different choline-deficient diet rats often (though by no means always) developed lesions resembling those of human arteriosclerosis. In the coronary arteries the changes closely resembled human atheroma: in the aorta they were more like Mönckeberg's sclerosis. But this finding must be interpreted with caution, since Wissler and his colleagues[9] in Chicago later produced rather similar lesions in rats by dietary variation, and claimed that in some circumstances the changes were made more severe by increasing the choline intake. Although there are differences between the two sets of experiments, this finding appears at first sight to contradict the Canadian work, and the matter requires further elucidation. Meanwhile, in 1945, Kesten, Salcedo, and Steffen[10] found that a choline-deficient diet to which ethyl laurate was added caused lesions of the myocardium in rats. They did not find the same result with fats other than ethyl laurate, and the observation seemed for a time to be of rather limited interest. However, in the present study, Wilgram, Hartroft, and Best found that, by varying the conditions of the experiment to allow more time for the lesions to develop, many other fats, notably lard and beef fat, can be used to produce similar changes, though these can always be prevented by adding sufficient choline.

The relevance of all this work to human cardiovascular disease has yet to be ascertained. If the dietary factors considered in this latest study are important, then we may perhaps congratulate ourselves on our wisdom in always taking eggs with our bacon; but it would be unwarrantable to draw any such definite conclusions in the present state of knowledge. Meanwhile, the Toronto workers are to be congratulated on a most valuable experimental investigation, and their further contributions will be eagerly awaited.

[1] *Amer. J. Physiol.*, 1922, **59**, 479.
[2] Ibid., 1924, **67**, 634.
[3] *Brit. J. exp. Path.*, 1924, **5**, 75.
[4] *Amer. J. Physiol.*, 1930, **93**, 657.
[5] *J. Physiol. (Lond.)*, 1932, **75**, 56.
[6] Ibid., 1932, **75**, 405.
[7] *Proc. Soc. exp. Biol. (N.Y.)*, 1939, **41**, 188.
[8] Ibid., 1952, **81**, 384.
[9] *Arch. Path. (Chicago)*, 1954, **57**, 333.
[10] *J. Nutr.*, 1945, **29**, 171.

REPORT ON GENERAL PRACTICE

The long-awaited report[1] on general practice by a committee of the Central Health Services Council of the Ministry of Health is published this week; a summary appears in the *Supplement*. Since the committee was set up under the chairmanship of Sir Henry Cohen in 1950 general practitioners must have become almost embarrassed by the limelight thrown upon them in the first quinquennium of the National Health Service. Two recent outstanding reports—by the B.M.A.'s General Practice Review Committee (including the Hadfield Survey)[2] and by Dr. Stephen Taylor[3]—have examined the situation so exhaustively that little new could be expected from the report now issued under the authority of the Central Health Services Council. Its value lies principally in the authority behind it, and in the fact that its conclusions have been reached only after the most painstaking sifting of the great volume of evidence put before the committee by many individuals and organizations, including, of course, the British Medical Association. In its inquiry "the committee has throughout had in mind that the general practitioner's work is closely bound up with all other aspects of the Service, preventive and curative, with hospitals, with local health authorities, with all the ancillary services, for instance nursing and midwifery, and with the school medical service." It sees general practice "as fundamental to the best practice of medicine and to the best interests of patients" and as something that "cannot be replaced by a congeries of specialisms." The

[1] Central Health Services Council. Report of the Committee on General Practice within the National Health Service. London: H.M.S.O. 1954. 2s. 6d. net.
[2] *British Medical Journal* and *Supplement*, September 26, 1953.
[3] See *British Medical Journal*, 1954, 1, 746.
[4] *The General Practitioner and the Hospital Service*. Edinburgh: H.M.S.O., 1952. Price 1s. 3d.
[5] "General Practice in America and Great Britain," *British Medical Journal*, June 19, 1954, p. 1391.

general practitioner is the one person who provides for continuity of treatment—no new observation, but one which needs constant repetition.

By July 1, 1952—the latest date for which full figures are available—20,162 doctors were engaged in general practice in England and Wales, 18,096 of them being principals, 1,689 assistants, 309 trainees; 68 were providing maternity services only. There were some 9,745 practitioners working in partnerships of various sizes, and the committee notes that provisional figures for 1953 show that partnerships are on the increase, accounting now for over 60% of the total of doctors in general practice. The growing formation of partnerships is one of the signs of the increasing co-operation among doctors in the N.H.S., a co-operation manifested also by the formation of rotas to provide services at night and during the week-end. The extension of co-operation is seen, too, in the increasing emphasis given to group practice, which makes for economy in effort by providing ancillary help and enables practitioners "to exercise some special skill to a degree which would not normally be expected in general practice." This development of special interest would be encouraged by the appointment of general practitioners to clinical assistantships in hospital, as advocated by the committee, which endorses the recommendations on this of a committee of the Scottish Health Services Council.[4] Group practice, according to the committee, means medical practice "carried on by several general practitioners working together in close association, consulting one another about their patients, and doing their 'surgery' work in whole or in part of a common building controlled by the doctors." They should work in common premises even if on occasion they also work in branch surgeries. A group should, the committee considers, consist of three to six principals. The advantages coming through such co-operation were seen as one of the strongest arguments for health centres, advantages the committee believes could be more easily secured through the evolution of group practices.

This is a shift of emphasis of much importance, and the committee makes the interesting suggestion that "a group practice might develop into the natural focus . . . of the various domiciliary arms of the Health Service." The sign-post is moved from the health centre owned by a local authority to the group practice owned and manned by general practitioners. Such a development would make it possible not only to employ adequate ancillary staff but also to provide proper accommodation and equipment: "Independent observers have been shocked by the low standards of accommodation and equipment provided by some doctors in some areas, particularly in industrial practice." No one can feel content with such a sorry state of affairs, on however limited a scale. In his recent article[5] Dr. Charles M. Fleming said that the three-roomed suite—waiting-room, consulting-room, and examination or treatment room—is regarded in the U.S.A. as "the basic minimum." We have much leeway to make up in this respect.

With all the benefits that would appear to flow from group practice, especially in the way of efficiency and economy, the advocated closer association of general practitioners with hospitals and with the work of local authorities should become so much the easier. Apart from these aspects of a doctor's work the committee considers many other details which will be read with interest by general practitioners—on methods of remuneration, on prescribing, on entering practice, on an appointments system, and so on. The committee's report is in effect a most valuable summing-up of the ideas and debates on general practice that have been to the fore since July, 1948. The problems that have arisen and the defects discussed are only in small part related to the National Health Service. They are inherent in the situation of general practice during a scientific and social revolution. The N.H.S. has compelled everyone to look at the whole matter with an inquiring and critical eye, and out of the inquiries a constructive approach emerges which is full of hope for the future of this important branch of medicine.

TREATMENT OF STREPTOCOCCAL TONSILLITIS

When a disease is short-lived and self-limiting, it is easy to form clinical impressions that one treatment or another is helpful, but difficult to prove that any is specific. Anderson *et al.*,[1] for example, and Macdonald and Watson[2] showed that the popular impression that sulphonamides were effective in the treatment of streptococcal tonsillitis was not based on fact, and they recommended that, because of possible toxicity, they should not be used as a routine. Since then antibiotics have been more freely used. Denny *et al.*[3] compared the effects of penicillin, aureomycin, and terramycin. They gave 600,000 units of procaine penicillin G daily for five days, and 1 g. of aureomycin or terramycin on admission followed by 19 six-hourly doses of 0.5 g. Though within five days the untreated disease might well be expected to resolve, the authors claimed that all three drugs relieved sore throat and headache but had no effect on chilliness. Aureomycin increased vomiting, and both aureomycin and terramycin caused some diarrhoea. Apart from toxicity, they conclude that there is little to choose between the drugs in their effect on the course of the disease, although elsewhere Denny[4] has reported that penicillin is more effective in clearing streptococci from the throat. There is evidence that

the rate of clearance of streptococci is related to the suppression of the rise in antistreptolysin titre and to the incidence of rheumatic fever following streptococcal infection. Houser *et al.*[5] investigated the use of aureomycin in the treatment of streptococcal tonsillitis and pharyngitis with special reference to this. They treated 1,009 adult patients with aureomycin for periods varying from four to six days and with total doses of 8–11 g. Comparison of results with those from 1,035 untreated controls showed that aureomycin caused a decrease in the carrier rate of haemolytic streptococci and a reduction in antistreptolysin formation. As to rheumatic sequelae, of 944 treated patients 5 developed rheumatic fever within 35 days of the streptococcal illness, and 11 within 45 days, while, in the untreated group, the figures were 20 and 24. Comparing these results with a previous trial of penicillin by Wannamaker *et al.*,[6] in which Houser and his associates took part, they concluded that penicillin was more effective than aureomycin in the clearing of streptococci, the suppression of antistreptolysin formation, and the prevention of rheumatic sequelae: of 978 penicillin-treated patients, 2 developed definite rheumatic fever, while of 996 untreated controls 28 did. Two injections of 600,000 units of depot penicillin given 72 hours apart were recommended. The writers of both reports[5 6] emphasize that elimination of streptococci from the throat is necessary if the maximum suppression of antistreptolysin production and of rheumatic sequelae is to be achieved. Penicillin appears to be most effective in this respect.

In the prevention of recurrences in patients who have already had rheumatic fever, Massell *et al.*[7] reported success with penicillin. Of 46 such patients who developed streptococcal infections, 34 were treated with penicillin and 12 had no treatment. Rheumatic fever recurred in 2 of the 34 treated and in 6 of the 12 untreated patients. Penicillin was given for 10 days, in most cases by mouth in doses of 1,000,000 units daily, a point of importance with regard to treatment in general practice. Penicillin troches have also been used to prevent rheumatic relapses, and Maliner[8] claims success by giving troches daily throughout winter, but it is not claimed that such treatment would be effective in acute streptococcal attacks.

From the available evidence it would appear that it is well worth treating streptococcal tonsillitis with penicillin. Some improvement in the patient's symptoms will usually result, but in addition the danger of rheumatic sequelae will be considerably reduced. In patients who have already suffered from rheumatic fever the need for penicillin is more urgent. As to mode of administration, while injections are surer, oral therapy is more convenient. Dosage must be adequate, not less than 400,000 units of crystalline penicillin G given three-hourly. Aqueous solutions are unfortunately not stable for long outside a refrigerator,[9] and instead the newer but much more expensive benzethacil suspensions, in doses of 300,000 units six-hourly, will give satisfactory serum levels.

[1] *British Medical Journal*, 1951, **1**, 326.
[2] Ibid., 1951, **1**, 323.
[3] *Pediatrics*, 1953, **11**, 7–14.
[4] *Postgrad. Med.*, 1953, **13**, 153.
[5] *Pediatrics*, 1953, **12**, 593–606.
[6] *Amer. J. Med.*, 1951, **10**, 673.
[7] Ibid., 1951, **146**, 1469–74.
[8] *J. Pediat.*, 1950, **37**, 858.
[9] *Pharm. J.*, 1954, Series 4, **118**, 229.

INTRAGASTRIC TEMPERATURE

The fictitious assumption of a constant blood temperature dies hard, and it is only in recent times that the significance of temperature gradients has been appreciated. Tissue respiration is directly dependent on blood flow, which varies according to the different degrees of activity of a tissue or organ. A change in temperature follows on any regional change in blood flow, so that if the blood volume and rate of flow to an area are increased the temperature will rise also.

Benjamin and others[1] have recently been investigating the relationship between intragastric temperatures and the stomach's vascular pattern. They found that the average stomach temperature was 1° to 3° F. (½ to 1½° C.) higher than the oral temperature. Hepburn[2] and his associates found similar results and reported the temperature of the small intestine to be about the same as that of the stomach, but in the large intestine it was 2° F. (1° C.) higher. Benjamin *et al.* used eight separately insulated thermocouples to produce a thermopile, which was conducted to a fixed cold junction in a vacuum flask. The thermopile was connected by two leads, well insulated, to a potentiometer with a twenty-four hour automatic recorder. The tips of the thermocouples were insulated and connected to a rubber balloon containing 5 ml. of mercury. The thermopile was passed through the nose and the weighted rubber balloon carried it into the stomach. These workers found that half an hour after normal individuals began to desire food the temperature took a sudden dip, thereafter becoming raised to its former level. They postulate that this was due to muscular contractions of the stomach arresting the blood flow, resulting in oxygen lack and a reduction in regional metabolism. They believe that this occurs through the same mechanism which Christensen[3] found in the finger. Christensen showed that at the beginning of heavy work there is a sudden and marked reduction in the skin's circulation, which lasts a few minutes before vasodilation occurs. He thought that at the start of heavy work the instantaneous and vigorous reduction of the blood in the finger was a regulating mechanism for adjusting the circulation from rest to heavy work. He considered this mechanism to be of nervous origin.

Benjamin[4] has suggested in an earlier paper that in the stimulated stomach the mucous membrane is kept in a state of anaemia owing to a diversion of blood to other organs. This is made unlikely by the work of Barclay and Bentley,[5] of Oxford, and Barlow, Bentley, and Walder,[6] of Newcastle, who have shown that the shunting phenomenon occurs mainly within the stomach wall through arterio-venous anastomoses, of which the

[1] Benjamin, H. B., *et al.*, *Surg. Gynec. Obstet.*, 1953, **97**, 19.
[2] Hepburn, J. S., *et al.*, *Arch. intern. Med.*, 1933, **52**, 603.
[3] Christensen, E. H., and Nielsen, M., *Acta physiol. scand.* 1942, **4**, 171.
[4] Benjamin, H. B., *Surg. Gynec. Obstet.*, 1951, **93**, 672.
[5] Barclay, A. E., and Bentley, F. H., *Brit. J. Radiol.*, 1949, **22**, 62.
[6] Barlow, T. E., *et al.*, *Surg. Gynec. Obstet.*, 1951, **93**, 657.

maximum size is about 140 μ. Benjamin found that in animal experiments the temperature fluctuations varied directly with the blood flow and oxygen consumption of the region. They examined a number of patients with proved gastric ulcers; the temperature variations were related to the activity of the ulcer. Ulcer activity was associated with hyperactivity of the stomach, hypersecretion, increased blood flow and oxygen consumption, and a rise in temperature. A cascade drop in temperature occurred as soon as a desire for food was expressed.

SEX DIFFERENCES IN POLYMORPHONUCLEAR LEUCOCYTES

For a long time the geneticists have insisted that so far as chromosome content is concerned the qualities of "maleness" and femaleness" must be projected from the fertilized ovum into the somatic cells. In 1949 the truth of this inference was very clearly and almost unbelievably demonstrated in ordinary tissue sections stained by simple dyes and examined by any serviceable compound microscope. This was achieved by Murray L. Barr,[1] professor of microscopic anatomy in the University of Western Ontario, London, Canada. He demonstrated a small, easily identifiable intranuclear body, staining intensely with basic dyes, in 35% of all resting nerve cells in sections of the brain and spinal cord of female cats. A far smaller and far less intensely staining intranuclear body was very occasionally identified in the nerve cells of male cats. The deeply staining and exclusively female structure was intimately associated with the nucleolus, which in nerve cells is exceptionally large and intensely basophilic. Barr named it the "nucleolar satellite," and this structure has now been identified in skin[2] and other tissues, and its presence in the nuclei of an adequate number of the cells in a section is a sure proof that the tissue came from an adult female mammal.

It is very probable that Barr's nucleolar satellite, found exclusively in the cells of females, is a mass of sex chromatin. The chromosomes of the nucleolus are frequently sex chromosomes and the X chromosomes are duplicated in the female cell. They are therefore likely to be closely related to the nucleolus. Furthermore they are endowed with more chromatin and therefore stain more deeply than the XY chromatin complex of the male cell, probably because of the small size of the Y chromosome.

Drs. W. M. Davidson and D. Robertson Smith, working at King's College Hospital, London, have extended Barr's observations in an attempt to "sex" a large number of blood films, and their investigations are reported in this issue of the *Journal*. They discovered that a nuclear appendage, strictly comparable in size and staining reaction with Barr's nucleolar satellite, was present in approximately 13 per 1,000 of the polymorphonuclear leucocytes in each female blood film. No "satellites" were seen in blood films taken from a large number of males. The sexing of skin biopsies has been used by Barr as an aid in the differential diagnosis of the various types of hermaphroditism, and Davidson and Smith's discovery may make such studies easier to carry out. Apart from its obvious biological interest, Scotland Yard is very likely to be stirred by this recent product of cytological research.

[1] *Nature, Lond.*, 1949, **163**, 676.

[2] Barr, M. L., Bertram, E. G., and Lindsay, H. A., *Surg. Gynec. Obstet.*, 1953, **98**, 641. See annotation in *British Medical Journal*, 1953, **2**, 387.

A PENICILLIN ANNIVERSARY

On May 10, 1929, the editors of the *British Journal of Experimental Pathology* received for publication a paper on the antibacterial action of cultures of penicillium. The silver jubilee of this great discovery was fittingly celebrated last Tuesday morning at St. Mary's Hospital Medical School by a presentation to the author of the paper, Sir Alexander Fleming, F.R.S. The presentation was made by the Duke of Edinburgh in the presence of members of the Medical School Council, the Wright-Fleming Institute Council, the Academic Board, and other guests. The Earl of Verulam, president of the Medical School, said that this year saw not only the silver jubilee of the discovery of penicillin but the centenary of the school. Although it nestled in the sophisticated precincts of Paddington, the school was ever conscious of its allegiance and the debt it owed to the mother University in Bloomsbury. The discovery of penicillin in 1929 was the outstanding work of a great scholar and member of the school, and his colleagues at St. Mary's had decided to make him a presentation in appreciation of his great services to mankind. He read telegrams of congratulation which had been received from the Senate and staff of Edinburgh University and from the Students' Representative Council. The Duke of Edinburgh, in presenting Sir Alexander Fleming with the gift—a pair of Georgian silver sauce tureens—said that he was in no position in that company to explain what Sir Alexander had done. But he knew enough about it to hope that he himself would never have to make use of the discovery. He was particularly delighted as Chancellor of the University of Edinburgh to make this presentation to its Lord Rector.

Sir Alexander Fleming spoke of his association with colleagues at St. Mary's past and present, and particularly of his indebtedness to Sir Almroth Wright, perhaps the greatest man to work in that hospital and medical school during the hundred years of its history. The discovery of penicillin, Sir Alexander Fleming added, had brought him unsought publicity and had completely destroyed his private peace. But it had had its compensations. He had received honours from many parts of the world, and now this wonderful present from his colleagues in the school. He concluded by taking from his waistcoat pocket a mounted specimen of the original mould *Penicillium notatum* from a culture of which penicillin had been filtered, and handed it to the Duke of Edinburgh, saying that he had already presented a specimen to the Queen Mother.

CLINICAL PATHOLOGY IN GENERAL PRACTICE

POST-MORTEM TECHNIQUE FOR THE OCCASIONAL PERFORMER

BY

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In Britain, where the services of a pathologist are usually readily available, the general practitioner will seldom feel justified in performing a post-mortem examination. However, occasionally he may have to do so, and this article sets out to describe how the examination should be conducted. If the necropsy has not been ordered by the coroner, the consent of the nearest relative should always be obtained. In addition, details of the circumstances of the death and of the previous medical history are of the greatest value in suggesting what abnormalities should specially be sought. Whenever possible the examination should be deferred until this information is available. The following description applies particularly to cases of sudden death in an adult, but the principles are the same for most post-mortem examinations.

Mortuary and Equipment

It is wise to be sure that the examination is to be carried out under tolerable conditions. The days are gone when a post-mortem examination must perforce be done on a kitchen table or in an unadapted outhouse. Good lighting, a proper examination table, adequate hot and cold water, and some source of heat are needed; refrigerated storage space is desirable, especially in the summer months. Most local authorities do not now demur at the cost of moving a body to some suitable mortuary. In addition to premises, a reliable mortuary attendant should be available to assist. Long experience has taught me that a good one is more valuable even than instruments.

An elaborate battery of instruments is not needed. The following will be found satisfactory:

Knives: two about 6 in. (15 cm.) long, of cartilage type; a long bacon-slicer type (or bread-knife) for cutting the brain; two or three scalpels, for preference of the type with detachable blades; a small bistoury. Scissors: one large pair, 7 in. (18 cm.) long; one pair 6 in. (15 cm.), blunt-ended; one pair, intestinal pattern, in which one blade is guarded; one or two small pairs for such purposes as opening coronary vessels, etc. Forceps: at least two pairs, preferably toothed. Butcher's saw about 10 in. (25 cm.) in length. Blunt chisel and mallet. Soup ladle for removing body fluids. Coronet, especially needed by a tyro. Probes, large and small. Bone-cutting forceps. Steel tape-measure. Scales and weights—preferably registering in grammes.

In addition containers for bacteriological and other specimens, suture materials, and protective clothing will be required, as follows:

Throat swabs. Small sterile containers for C.S.F. and urine. Catheters. Clean slides. Specimen tubes. Sterile syringes and needles, including lumbar-puncture needles. Suture needles—3 in. (7.5 cm.) curved type I find most suitable. Thread—upholsterer's twine. Tow. Sponges—at least two. Surgeon's gown. Rubber apron and Wellingtons or rubber overshoes (desirable but not essential). Mask if necessary. Spectacles—desirable. Gloves: individual preference plays a part here. I recommend the thin "latex" gauntlet type, which are most comfortable if secured by an ordinary rubber band just below the elbow, and cotton overgloves. Two pairs of gloves may sound clumsy, but they are safe and efficient, as the cotton provides a better grip on slippery organs. Ordinary surgical gloves will suffice alone. Some pathologists prefer the standard rubber gauntlet gloves.

A note-book or slate must be available, and it is a wise plan to list the salient features to be noted on this before the examination begins.

Sudden Deaths

A check on my own figures shows that approximately 75% of these are due to natural causes and 20 to 25% are accidental or criminal cases (mainly accident). Of the 75%, about 40% are related to some defect of the coronary arteries, be it occlusion, thrombosis, or a complication, cardiac infarction, or cardiac rupture; 15% are due to cerebral haemorrhage or thrombosis, including subarachnoid disasters. Other common causes are massive haemorrhage and "syncope." This last presents no specific findings and may need to be inferred from the absence of pathological evidence and the general circumstances. In susceptible persons reflex vagal inhibition sometimes follows comparatively minor procedures affecting the skin, pleura, peritoneum and the vagina (a pitfall for the abortionist). Concussion, although showing changes discernible microscopically, may show little or nothing to the naked eye. A blow over the heart may be fatal and is not uncommon in, for example, steering-wheel injuries. Poisons must never be forgotten in cases of sudden death, especially carbon monoxide and coal gas. Inquiries should be made regarding the possibility of this, and a sample of blood taken for test. (The container must be completely filled.) The commonest poisons met with in practice are the narcotics, and these should be considered in cases in which the obvious findings are cyanosis of the ears, lips, lungs, etc., without pathological explanation.

With these preliminary remarks the actual examination can now be described.

First inspect the body externally and make notes of identification—for example, height, approximate weight, scars and other marks (tattoo designs), presence or absence of false teeth, etc. Note the degree of rigor mortis, the state of general nutrition, and colour. Any departure from normal must be recorded—slight yellow staining on a man's hand proved on inquiry to be due to the toxic weed-killer dinitro-*ortho*-cresol, and a factor in the death. A splinter beneath a toenail has yielded tetanus bacilli; a small "boil" proved to be an anthrax pustule. Inspect the eyes and the ears. Embarrassment can be caused if at an inquest questions are asked about possible blindness or deafness, which could easily have been answered by observing the presence of a glass eye or an old mastoid wound. Always turn the body over. This may sound obvious, but I have known bedsores to be overlooked because of its omission.

In many cases I make a routine procedure of doing a post-mortem lumbar puncture, which is generally easy, even in the presence of rigor mortis. Fulminating meningitis, intrathecal haemorrhage, etc., may be detected, whilst even a normal fluid may yield barbiturates more easily than, for example, urine. Pathological findings in the spinal fluid after death are not exactly parallel to those in life. The cell count in particular is deceptive, as theca cells are shed and give a falsely high figure. Of course, after death there is no spinal fluid pressure and suction with a syringe is needed.

Brain and Spinal Cord

I was taught to begin by opening the skull, on the grounds that if the body were opened first loss of blood from the great veins would change the appearances of the brain. I am not convinced that this is entirely true, but every case should be considered on its merits. The hair is parted across the vertex from just behind the ears, and the scalp cut through to the bone. The two flaps are then reflected, the front one forwards to just above the orbits and the posterior one to the occiput. Cut through the temporal muscles and then place the coronet in position as a guide for the saw cut. The saw should be used a little at a time, so that the depth of the cut right round the skull is approximately the same. When the inner table is reached, provided a fracture of the skull is not suspected, the skull cap can be most quickly removed by using a chisel. The dura is incised along the line of the cut, but in some cases it is very adherent, and then it is necessary to remove it with the bone.

To remove the brain, pull gently on the frontal lobes and sever the cranial nerves. Cut the tentorium with a scalpel (if a bistoury is available this is preferable). If the spinal cord is not required in continuity this is incised just below the medulla and the brain removed. If microscopical examination is intended the brain should be placed in a 5% formol saline fixative for at least several days, but in the ordinary way this is not necessary and the brain should be cut. Provided the same general method is used on every occasion no set procedure is needed. It is only necessary to ensure that each part of the brain is inspected in turn. My own method is to examine the organ carefully externally, looking at the vessels and the fissures, especially the fissure of Sylvius, where, for example, tubercles might be found, and then with a large bacon- or bread-knife, which should be used wet, a cut is made horizontally about ¾ in. (2 cm.) deep right through the upper part of the cerebral hemispheres. The next cut can be parallel with this and should open the lateral ventricles. Transverse incisions about ½ in. (1.3 cm.) apart will enable the basal ganglia to be examined. Next the cerebellum should be cut in the midline, and on opening out the cut the iter and fourth ventricle are viewed. The cerebellum is removed, and then transverse cuts should be made in the brain stem. A small lesion here may produce large consequences, and therefore the cuts should be close together.

Although perfection demands that the spinal cord should be examined in every case this is usually done only in cases in which the history or the examination itself indicates the necessity. To do so the body is turned over, face downwards, and with the head over the end of the table, or with a block under the chest. An incision is made over the vertebral spines and the muscles on either side are cut away to expose the laminae. These are then divided with a saw or with bone forceps. The spines and laminae and attached ligaments are then cut away, opening up the spinal canal. The cord is removed by cutting the spinal nerves. More usually the cord is severed in the cervical region, but if it is desired to remove it in continuity with the brain, the edges of the foramen magnum are cut away by sawing through the occiput on either side. To examine for a fracture of the base of the skull the dura must be stripped. Care is needed not to mistake vascular markings for a fracture. Hold the skull cup up to a strong light to inspect this; tapping its edge will yield a cracked-pot sound if a break is present.

The middle ear can be opened by driving a chisel through the tegmen on either side. To examine the pituitary cut away both posterior clinoids with a chisel. The antra may be reached through the anterior fossa.

Opening the Thorax and Abdomen

Stand on the right side of the body and make an incision from the point of the chin down to the pubes. In the neck the skin only is incised, over the chest cut down to the bone, in the abdomen cut through to the peritoneum, taking care not to injure a viscus. In the abdomen first make a small hole and look to see that no viscera or omentum are in the way before extending the peritoneal incision. I make a routine of cutting the abdominal recti close to the pubic attachment, as this allows the abdominal wound to be more widely opened. The soft parts over the chest are stripped back over the costal cartilages to approximately the outer edge of the clavicle. Before doing more, preliminary inspection should be made of the abdominal contents and the pelvis, and a note taken of the position of the diaphragm. In women past the age of 35 the mammary glands are examined by cutting them from the inside of the flaps without injuring the skin if possible. This is done so that small carcinomata shall not be overlooked. The costal cartilages are cut with a knife, except in the elderly, in whom bone forceps or a saw may be needed. The sterno-clavicular joint is disarticulated and the sternum and attached costal cartilages are removed. The pleural cavities can then be examined for adhesions, fluid, presence of lung collapse, ballooning, etc. The pericardium is inspected and opened.

At this point I open the pulmonary artery and its main branches, and look for emboli. Post-mortem clot must not be mistaken for this. An embolus is fairly firm, very often presenting a "mare's tail" appearance if it comes from the legs. A simple test, which is of value when in doubt, is to take the clot and place it in water. Post-mortem clot will easily break up, but an embolus does not do so. If an embolus is found, search must be made for its origin. Usually this is in the leg, the pelvis, or sometimes the abdomen. It is not always possible to find the site, but often there is roughening of the vein wall at the point of origin, and sometimes further ante-mortem thrombus is still adherent to the vessel wall.

It is best to remove the tongue, fauces, larynx, trachea, and oesophagus *en bloc* with the thoracic viscera. Dissect the skin away from the submental region and cut close to the jaw into the floor of the mouth. The tongue can be hooked forward with the left hand and the posterior attachments, including the carotid vessels, freed with a knife. By pulling forward, the next main lines of attachment are displayed—the great vessels at the root of the neck, which, when cut, allow the lungs to be pulled out provided there are no pleural adhesions. If there are, they should, of course, be broken. It is wise to ligature either the oesophagus or the oesophageal opening in the diaphragm in order to preserve the stomach contents. The thoracic viscera may then be removed by cutting through the aorta, oesophagus, inferior vena cava, and base of the pericardium.

Thoracic Viscera

To examine the thoracic viscera, the pharynx and oesophagus are first slit with scissors and examined, the condition of the tonsils and tongue, which will show significant changes, for example, in cases of corrosive poisoning, being noted. The larynx, trachea, and main bronchi are opened, also with scissors, and the contents inspected—for example, for mucopus, oedema fluid, and foreign substances.

The lungs can then be examined and cut through from the outer edge to the hilum, with subsequent cuts where necessary. Portions of the lung which appear solid should be tested by placing them in water. Anything which is thought to be abnormal should be opened up and examined. Note should be made of enlarged mediastinal glands. In the case of tuberculosis, great care should be taken to avoid splashing (a mask should be worn). Even when care has been taken in cutting a tuberculous lung, minute splashes may deposit tubercle bacilli on a glass plate held a foot (30 cm.) away.

Examination of the heart, apart from being of great importance, seems to cause difficulty to beginners. If it is remembered that both auricles and ventricles must be opened, and that the condition of all the valves, the heart

muscle, and the coronary arteries must be ascertained, it is not difficult to adopt a system. First, the right auricle can be opened by cutting from the superior vena cava to the inferior vena cava, with an incision at right angles from this into the right auricular appendix (search for thrombi); any clots should be washed away, and the tricuspid valve, which normally admits about three fingers, should be inspected. Each cusp should be examined for vegetations and scarring. The left auricle is opened by cutting between the two upper pulmonary veins and continuing this incision into the auricular appendix. Again look for thrombi, vegetations, and possible thickening of the endocardium. The mitral valve can be inspected from above, and normally admits one finger with ease and two with difficulty.

The right ventricle may be opened by an incision down from the pulmonary artery parallel to the interventricular septum but anterior to it, and the state of the contents observed. The pulmonary valves may first be tested with water and inspected. The left ventricle can be opened by an incision in its lateral aspect, and an incision at right angles to this, right across the apex, will indicate the thickness of the muscle. The aortic valve can be water tested, looked at from above, and scissors passed down from above through the valve across to the left ventricle, laying open the valve and ventricle in continuity. Alterations in the valve cusps and the state of the aortic ring are very easily observed. The orifices of the two coronary arteries should be examined. The right coronary artery rises from the right antero-lateral sinus of Valsalva and is smaller than the left. It supplies most of the right ventricle and auricle, together with a part of the left auricle. The left coronary artery, rising from the left antero-lateral sinus of Valsalva, divides into two main branches, which together supply most of the left ventricle, the interventricular septum, and also a small part of the right ventricle and the lower third of the left auricle. The main division is the descending branch, which passes down the anterior interventricular groove, and it is this branch which is most commonly affected by disease, the most frequent site for thrombosis, degeneration, or occlusion being 1 to 1½ in. (25 to 38 mm.) from the aortic valve. The other branch runs back in the auriculo-ventricular groove to supply the posterior part of the left ventricle.

It is possible to open up the coronary arteries with fine pointed scissors, but by so doing thrombi may be dislodged, and I think it preferable to make frequent cuts at right angles to the vessels with a sharp scalpel or even a razor blade. The state of the lumen can be seen at each point, and if desired the short intervening lengths may be opened with scissors. In an area of infarction the appearances vary with the time since its occurrence. For a few hours almost nothing may be visible to the naked eye, though later the infarcted area becomes swollen and shows a red haemorrhagic demarcation. If the whole thickness of the heart muscle is involved an adherent thrombus is commonly seen in the cavity involved. Ten to fifteen days after infarction organization becomes apparent, and later this granulation tissue is changed to fibrous scar.

The thoracic aorta must next be opened and inspected for degeneration. Syphilis, now becoming increasingly rare, commonly produces distortion and often dilatation of the first part of the aorta, with replacement of adventitia, media, and intima by vascular granulation tissue. Pearly white scars, often around the vasa vasorum, may produce puckering. Simple atheromatous degeneration frequently co-exists, and the yellow degenerate material can be seen if the suspected patch is cut across. It is often calcified.

Abdominal Viscera

First inspect to decide which method of approach is appropriate. Unless there is reason to suspect lesions in the small intestine this may be removed by cutting along the root of the mesentery with a sharp knife. The appendix should be examined and then the whole of the large intestine may be stripped away down to the pelvi-rectal junction, where it is cut. The small intestine can be freed by cutting across the duodeno-jejunal junction. If it is desired to retain the contents, string ligatures can be applied. Where the contents are not of significance the duodenum can be opened as far as its second part, when pressure on the gall-bladder should produce a flow of bile, indicating the patency of the ducts. Ligatures can then be applied to the upper and lower ends of the stomach and the organ removed whole. It is opened along the greater curvature, and the appearance and smell of its contents noted, as well as the possible presence of tablets, powder, etc. A sample of the contents can be retained in case analysis is required. The presence of ulceration, gastritis, or growth in the stomach wall is readily detected. In the case of intestinal disease the whole length of the intestine must be freed and opened with intestinal scissors along the mesenteric attachment. A flow of running water is needed for proper inspection.

The spleen, which may be removed with the stomach, should be examined for size, state of capsule, and possible infarcts. In cases of suspected septicaemia the surface should be seared with a hot knife or iron, and a swab pushed through the seared area into the pulp for subsequent bacteriological examination.

The liver and gall-bladder are removed and weighed, and the gall-bladder is opened. The liver should be cut at several points with sweeping incisions, using the bacon- or bread-knife.

The pancreas should be opened, preferably along the line of its main ducts.

The kidneys and suprarenals should be seen *in situ* and dissected away without cutting the ureters or vessels until these have been displayed. The kidneys should be freed of adherent fatty tissue and bisected with the bread-knife. A small point of technique which increases safety is to place the kidney flat on the table, cover it with a sponge, and hold it with the left hand, and then cut horizontally with the right hand. Not only is the grip on the organ firm, but the risk of cutting the hand is reduced. To cut towards the palm of the hand, as some books show, is in my view dangerous. Other small organs may be opened in the same way. The kidney capsule should be stripped away so as to inspect the underlying surface, and the state of the cortex, medulla, and pelvis noted.

The bladder should be opened, and the prostate palpated and removed if there is any abnormality. In women the pelvic organs should be removed *en bloc* together with the upper two-thirds of the vagina if this is indicated—a quite simple thing to do. If abortion is suspected the vulva and vagina must be carefully inspected from below before the pelvic organs are removed. In criminal abortion there may be evidence of local injury, peritonitis or other sepsis, and air or even foreign material like paraffin or glycerin may be found in the pelvic veins.

The testes may be drawn up by enlarging the inguinal rings. I have known of massive secondary deposits from a minute testicular primary tumour.

Special Investigations

The routine having been described, there are many other points to remember. If poisons are suspected and the coroner orders an analysis, an appropriate set of containers made of arsenic-free glass should be obtained. These are supplied by the Forensic Science Laboratories of the Home Office, and a set is held at most police headquarters. The organs should be submitted in separate containers as follows: (1) Stomach and contents. (2) Intestines and contents. (3) Liver. (4) Kidneys and spleen. (5) Brain. (6) Heart. (7) Lungs (sometimes). For transmission they must be sealed with some recognizable mark and if handed to the police a receipt must be obtained so that proof is available of every step in the procedure in the event of evidence being required in court.

Where bacteriological investigation is needed specimens are usually obtained with an ordinary throat swab. In suspected septicaemia it is customary to take cultures from the heart blood and from the spleen. In both these organs

the surface should be seared with a hot iron or knife, and incised with a sterile weapon through the seared area before the culture is taken. Urine may be obtained by catheter, or a sterile syringe and needle can be used to aspirate it direct from the bladder.

Certain conditions, not uncommon, may be missed unless specially looked for. Air embolism may be the cause of death in injuries to the neck veins, and occasionally after criminal abortion with a Higginson syringe. Bubbles of air may be visible in the meninges, and the presence of air in the heart can be detected by opening the pericardium, filling it with water, and then piercing the right auricle. Obviously, if decomposition has occurred the test is invalid. Fat embolism is a common cause of death in multiple bone injuries, and fat in the lung may be demonstrated quickly by Robb-Smith's technique. Tiny pieces of lung are treated on a slide with potassium hydroxide until the red blood cells dissolve, when the fat is visible in the pulmonary capillaries. My personal preference is to take organs, especially the lung, brain, and kidneys, to the laboratory and cut frozen sections to be stained with scharlach R. It is primarily the cerebral condition which is fatal, and this is beautifully shown by the frozen method.

Pneumothorax, if suspected, may be detected by putting water between the skin flap and the ribs, and opening an intercostal space with a knife and watching for the emission of air.

Conditions not specifically mentioned which may be missed are electrocution, be it from faulty apparatus or lightning discharge. Here small burns can be found, particularly at the entry or exit point of the current, while the clothes may be singed or even stripped off the body. I remember an example in which a bone and metal collar-stud disappeared except for the small metal portion, which was driven into the trachea.

Acute encephalomyelitis may be detectable only by microscopical examination of the brain, but a clue is often given by a definite increase in cells in the spinal fluid.

Thyroid conditions, whether toxic or myxoedematous, may be associated with sudden death, and myxoedema may be easily missed in menopausal cases unless the thyroid is examined microscopically.

Uraemia, usually associated with hypertension and kidney lesions, may be proved by analysis, and here again the spinal fluid seems to give reliable results.

Glucose estimations in deaths from diabetes are unreliable, owing to post-mortem glycolysis.

In injuries to the neck fracture may occur, with crushing of the spinal cord, and yet not be immediately visible owing to self-reduction. It will be revealed only by opening the cervical cord and by careful dissection.

Conclusion

It is quite impossible, in a limited space, to cover the whole field of post-mortem work, and I would conclude by giving the advice that the safest working rule is never to cut anything without first being sure that evidence likely to be needed later is not being destroyed. In addition, it is no bad plan to include in the post-mortem kit some handbook on the subject, of which I would mention particularly *Post-Mortem Appearances*, by Joan Ross, published by Oxford Medical Publications, and *Practical Pathology, including Morbid Anatomy and Post-Mortem Technique*, by James Miller and James Davidson, published by A. and C. Black. There are no doubt other publications equally valuable.

Refresher Course Books.—The first two volumes of collected articles from the Refresher Course for General Practitioners published in the *Journal* are now available. The first volume contains 55 articles and the second 60. Each article has been revised by its author. Copies of both volumes may be obtained, price 25s. (postage 1s.) each, direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers. The second book of "**Any Questions?**" is also available, price 7s. 6d. (postage 6d.).

EVOLUTION OF HOSPITAL AND LOCAL AUTHORITY ANTENATAL CARE UNDER THE N.H.S. ACT

BY

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Present-day antenatal care is becoming increasingly complex. To prevent overlapping of the services and to ensure that the expectant mother receives the best possible care it is essential that an integrated service, based on good team-work of all those concerned, should be established.

In this article attention is directed mainly to those expectant mothers who are to be delivered in hospital. The arrangements for antenatal care for such cases vary from area to area. The patient may attend an antenatal clinic held at the hospital. She may perhaps attend a local authority antenatal clinic situated at a distance from the hospital and be cared for by a medical officer of the local health authority, usually, however, being seen at least once during pregnancy by a consultant or some other member of the hospital staff. A third procedure is that a bed for the patient may be booked by a general practitioner merely by filling in a form; the antenatal care from then on will be in his hands.

Conditions of Antenatal Care

There should be firm links between the antenatal clinic and the hospital, so ensuring continuity of medical policy throughout the antenatal period, labour, and the puerperium to the post-natal visit. Moreover, the patient should know her medical attendants, who should try to know her as a person as well as deal with her medical problems.

Notes made during the antenatal period should be available in hospital when the patient is admitted either as an antenatal case or in labour.

The clinic should be so situated that there is no undue travelling on the part of the patient. Long waiting should be avoided, and the "sausage-machine" tactics of the larger clinics must be avoided. The atmosphere should be friendly and stress the normality of pregnancy.

Finally, such investigations by the obstetrician as may be required must be readily available and, wherever possible, they should be done at the clinic itself.

Application of these Conditions in Practice

(*a*) The antenatal clinic attached to the hospital could fulfil most of the conditions mentioned above more easily than by any other arrangement. Local factors, however, usually cause the hospital clinic to fall short of the ideal. For instance, it may be geographically difficult for the patient to reach the hospital. Another disadvantage is that, by the concentration of large numbers of patients, the clinic becomes unmanageable in size, with the result that there is prolonged waiting and loss of the personal touch.

(*b*) The local health authority antenatal clinic, being situated near the patient's home, is usually accessible and

the clinics are small and personal. The increased demand made on the consultant's time in having to visit these clinics is entirely outweighed by the convenience to the patient; but, as usually organized, the clinics have certain disadvantages. The local authority medical officer may never see the consultant or any member of the hospital staff, and may never see a delivery. The most serious objection of all, however, is that the notes taken during the antenatal period may not reach hospital before the patient is admitted and no record of the antenatal period is available to the obstetrician in charge of the delivery. In Bristol, efforts had been made to overcome this difficulty by sending to hospital a "photostatic" copy of the antenatal notes made at the 36th week of pregnancy. However, a patient might be admitted before her notes reached hospital; moreover, the vital entries of the last three to four weeks would not be available.

(c) If the patient attends her own general practitioner for antenatal care she is cared for by one who knows her medical history and social background; confidence and the personal touch are maintained and the patient will not have far to travel. Again, however, the question of antenatal notes and contact with the hospital is raised. The patient comes into hospital in labour as a stranger both from a medical and from a personal point of view. Also, the general practitioner working single-handed in his surgery may consider that it is a strain on his time to conduct the full range of investigations necessary.

A New Approach

A system has been evolved in Bristol to overcome the difficulties of each of the three procedures mentioned above. At least one session at the antenatal clinic is attended jointly by the consultant and the local authority doctor. This gives opportunity for an exchange of ideas beween hospital and clinic and the maintenance of a common medical policy. Also, a clinical meeting is held weekly at the hospital to discuss cases delivered during the week: many of the clinic doctors attend this meeting.

The consultant sees each case early in pregnancy as well as at the customary 36th week. Moreover, the combined clinic enables him to see a case in conjunction with the clinic doctor at any time, neither of them losing contact with or interest in the patient.

The problem of making the antenatal notes available in hospital is a difficult one, and the solution we have arrived at may still be somewhat unwieldy but it is less complicated in practice than it sounds in description. A system of duplicating notes is used, each form being attached to its fellow at the top edge by a line of perforations, with a piece of "one-time" carbon paper between. The top sheet is torn off and sent to hospital; the carbon copy is kept at the clinic as a permanent record. At the patient's first visit the clinic doctor takes the history and performs a general examination and the laboratory tests, such as the Kahn reaction, blood group, and haemoglobin estimation. When completed, the original form is sent to hospital, while the carbon copy stays at the clinic. The routine antenatal record is kept similarly on a duplicate sheet, and at 30 weeks' gestation the original is sent to the hospital as before. From the 30th week onwards a second sheet is instituted, to record the routine pregnancy findings, and in addition a summary of these is placed upon a "personal card" carried by the patient herself. On her admission to hospital in labour the patient's "personal card" will give all the information from the 30th week onwards, while the clinic notes prior to this have already reached the hospital. As soon as the clinic sister is aware that the patient has been admitted, she sends the remaining notes to the hospital to form part of the full in-patient notes. Should the patient be admitted to hospital from the antenatal clinic on account of some abnormality, the antenatal notes may be sent in with her, the copy remaining at the clinic.

After delivery a summary of the hospital treatment is sent to the clinic; it is also entered on the "personal card." The findings at the post-natal visit are recorded, again with a carbon copy, and sent to hospital. Thus the hospital and the clinic have a complete record of the case from the first antenatal visit to the post-natal attendance. The "personal card" has proved a most valuable link between the antenatal clinic and hospital. Lennon (1952) says: "I found by experience that patients very seldom forgot their cards, and, if they did, relatives brought them to the hospital very quickly. This 'personal card' is printed on both sides. It is a single card which is folded in two and enclosed in an envelope. On the outside of this envelope are instructions to the patient to carry the card with her in her handbag at all times, and there is also the address of a hospital or clinic to which the card should be returned if found. It is not intended that this card should replace the full clinic notes, but that it should be a supplement to these, . . . particularly in emergency."

Place of the General Practitioner in Antenatal Care

However well the foregoing procedure may work, and giving full credit to the local authority doctors for their contribution to the care of the pregnant woman, the ideal would be for the general practitioner to work in co-operation with the hospital staff in the management of his own pregnant patients.

We have now arranged that whenever a patient has been booked for hospital confinement through an antenatal clinic she is given a note to take to her own general practitioner informing him of this fact. This avoids the criticism, so often made, that the first intimation the general practitioner may have that his patient has become pregnant is when meeting her pushing a perambulator along the main thoroughfare.

At the William Budd General Practitioner Health Centre, which was opened in Bristol in 1952, certain general practitioners hold their routine surgeries: it is also used by a local authority antenatal clinic attended by a consultant from Southmead Hospital as well as by a local authority medical officer. It was apparent that here was the ideal situation for the general practitioner to take part in the antenatal care of his own patients, for the note system outlined in the previous paragraph was in operation in the same building. The general practitioners concerned have co-operated enthusiastically by starting a special antenatal clinic session on one afternoon where all the interested G P.s attend as well as the district midwives. To the general practitioner this means having at his disposal all the secretarial and nursing facilities of the centre. To the patient it means that her medical care, both general and antenatal, lies in one place and in the hands of only two doctors—her own general practitioner and the consultant. To the hospital it means continuity of medical policy, achieved by direct and personal contact between the hospital representative and the patient's own doctor.

A natural development of these arrangements is the consideration whether the same principle can be extended to other local authority antenatal clinics not planned as general-practitioner health centres. There seems to be no reason why it should not, provided the general practitioners who are interested in obstetrics in the area can agree upon suitable sessions at which they could all attend. This has, in fact, been started in Bristol at a clinic on the new housing estate of Lawrence Weston, and it is hoped that this practice will be extended.

Domiciliary Confinement

The same arrangements, both medical and administrative, are taking place in connexion with domiciliary confinements. If a case booked for delivery at home is diverted into hospital for medical reasons, all the necessary information is readily available.

The combined clinic at which both general practitioners and midwives attend should go a long way towards abolishing one of the most unnecessary controversies which have arisen in the practice of obstetrics. As all cases will be seen by the midwife as well as the practitioner, with the consultant on call as required, there ceases to be any question of whether a case is a midwife's delivery or a doctor's confinement, for the functions of midwife and general practitioner are complementary, as they should be, and in fact always have been.

The Clinic Doctor

What is the future for the local authority medical officer? Even assuming that much of the work in the antenatal clinics be taken over by the general practitioner in the way described, there still remain the patients of those doctors who are unwilling to undertake antenatal care. It is likely that such cases will be numerous, and change in the present system of antenatal care is likely to be gradual.

It would be churlish not to pay tribute to the work of the clinic doctors, who came into existence to provide adequate antenatal care at a time when this was not otherwise available, and it is no reflection on them to suggest that the work should be done by the patient's own general practitioner where this is feasible. Moreover, the local health authority should continue to provide very important educational facilities—by holding mothercraft classes, and antenatal exercise and relaxation sessions in the centre.

The developments outlined above have not come to pass through the efforts of any one person. Professor G. G. Lennon has striven hard to achieve a closer link between those engaged in antenatal care. Professor R. H. Parry, Medical Officer of Health, and the Bristol Health Committee, in conjunction with the Southmead Hospital Authorities, have willingly co-operated in the linking of the clinics with the hospital. In particular, the new note system has involved a good deal of work shared by the records officers of the local health authority and the hospital. The co-operation on the part of the general practitioners at the William Budd Health Centre and at the Lawrence Weston Clinic has made the work there a great pleasure. Finally, our thanks must go to all the local authority clinic doctors, midwives, and health visitors who have assisted in the development of the service.

REFERENCE

Lennon, G. G. (1952). *Publ. Hlth*, 65, 199.

Reports of Societies

LOCAL MEDICAL SOCIETIES

Liverpool Society of Anaesthetists and the Section of Anaesthetics of the Manchester Medical Society

At a joint meeting held in Manchester on April 8 Dr. A. R. HUNTER read a paper on the new short-acting hypotensive drug, "arfonad."

He said that hexamethonium was unsatisfactory for inducing hypotension, because the tachyphylaxis to it, which developed so rapidly, made it impossible to give the drug in fractional doses until the required degree of ganglion block for the individual patient had been produced. Arfonad, given in a drip in a 0.06 or 0.1% solution, was therefore tested as an alternative in 20 neurosurgical cases undergoing operations for aneurysm, angiomata, and vascular meningiomas. Arfonad proved to be quickly acting, but a safety pause of five minutes was needed after the blood pressure had begun to fall. Tachyphylaxis was encountered, but this difficulty could be overcome by giving large amounts of the drug. When the hypotension was no longer needed the blood pressure could readily be restored to normal on stopping the drip, by inversion, or the injection of methylamphetamine hydrochloride, or both.

The only complication directly traceable to the arfonad was the appearance of a red streaking of the skin overlying the vein into which the drug was being run. Two patients died in the post-operative period, but the deaths would have been by no means unexpected had no hypotension been induced. The following danger signs were noted during arfonad hypotension: gasping respiration seemed to indicate acute medullary anoxia, and congestion of the operation area, with local venous bleeding, that the oxygenation of the myocardium was being interfered with. Excessive reduction of the haemoglobin in the cerebral veins was assumed to signify slowing of the blood flow to such an extent that cerebral anoxia had begun to develop. Arfonad was more potent than hexamethonium, and it had less cardio-accelerator action. It reduced the risks of hypotension in cases where this technique was essential, but did not make hypotension safe for everyone.

Manchester Medical Society

At the annual general meeting of the Manchester Medical Society on May 5, Sir HENEAGE OGILVIE gave an address on "The Future of Surgery." He said that writers in the past had thought that surgery had no future and that its role remained to polish and perfect what had already been done. As regards operative surgery this might be to some extent true, for technical skill had not improved in the last 50 years. Yet in those 50 years new operations had been invented, new parts of the body had been explored, operative mortality had fallen, and operative results had improved. This advance had been due not to surgical skill or enterprise but to advances in para-surgical methods, particularly in anaesthetics. Manual skill could not improve much further, but this was not the whole of surgery or even its most important part. The worst surgeons were nearly all good operators. The great surgeon must have, in addition to skill, knowledge, wisdom, clarity of thought and diction, originality, leadership, integrity, courage, and above all humility, without which no advance was possible. Increase of skill could come by the division of labour in an operation, particularly by handing over parts of it that involve difficult stitching to a nurse.

Two things surgeons would like to have, Sir Heneage said, were a contrast medium excreted by the pancreas, and a systemic haemostatic, able to seal cut vessels but not liable to produce clotting in intact ones. The avoidance of blood loss by retarding the circulation might be valuable in certain difficult operations, but it carried too great a risk of producing thrombosis in the cardiac and cerebral vessels to justify its extended use at the present time.

The prospects for the future of surgery as a profession were not encouraging, he continued. All important advances in surgery had come from Britain, because the door was always open to let in those who were on the way up, to let out those who were on the way down, and to offer a broad hint to those who were merely starting. Now, in place of surgery as a vocation, a dangerous adventure calling to the stout of heart, we had surgery as a guaranteed career, calling to those in search of security. The pre-Beveridge surgeon was offered an opportunity only, and he had to make it into a position and a livelihood by his own efforts. The contemporary surgical aspirant walked into a board-room a registrar and walked out a consultant—made for life. The present position did not recognize the fact that surgery is a profession in which skill and wisdom are acquired slowly, progressively, and by apprenticeship, and that a far more gradual release of supervision and assumption of responsibility are required.

North of England Society of Anaesthetists

At the final meeting of the 1953–4 session, on May 21, the president, Dr. E. J. MILLAR, presented the Registrar's Prize to Dr. F. SORRELL for an essay entitled "Some Aspects of Bronchospasm." Dr. M. H. ARMSTRONG DAVISON was elected president for the coming session and Dr. E. I. TATE was re-elected hon. secretary.

SIR ROBERT MUIR, 90

Students and former students of the Glasgow School of Pathology, and indeed pathologists everywhere, and not only in this country, will join in congratulations to Sir Robert Muir on July 5 when he celebrates his ninetieth birthday. It is 18 years since he resigned his chair and became professor emeritus at Glasgow, but the work he did in the Pathological Institute of the Western Infirmary, where his bust, by G. H. Paulin, looks down on successive generations of students, lives after him. His textbooks, the first of which, *A Manual of Bacteriology*, was published in 1897 and reached its tenth edition 40 years later, are still the grammar of the pathological student. On the occasion of his seventieth birthday 20 of his former students, including 11 professors of pathology, contributed to a *Festschrift* in his honour. He had been foremost in securing the recognition and independence of the study of pathology and its proper place in the medical curriculum.

Honours have come to Sir Robert Muir from far and wide. Glasgow, where he made his name, has made him an honorary LL.D. Similar distinctions have been accorded him by the Universities of Bristol, Durham, and Leeds. He has been the recipient of the Royal Medal of the Royal Society, of which he has been a Fellow since 1911; of the Honorary Fellowship of the Royal College of Physicians of Edinburgh; and of the Lister Medal of the Royal College of Surgeons of England. Of this last he was the first recipient who was not a surgeon. Twenty years ago he received the honour of knighthood. All this and much more is an indication of the value of the contribution which he has made to pathological research, to his pioneer work in the study of immunity reactions and mechanisms, and to the leading part he has taken in laying the foundations of the science of immunology. Muir's name stands at the beginning of a memorable chapter in medical history.

But perhaps in his retirement his thoughts go back to the manse on the Scottish Border where he spent his boyhood, to the Academy at Hawick where he went to school, and to the University of Edinburgh where he took his M.A. 70 years ago and his M.D., with a thesis which earned him the gold medal, six years later. It was in that environment that he acquired the knowledge and skill which enabled him to undertake research and to teach with authority, but it was there also that he developed those personal qualities of sympathy and generosity which have made his teaching so memorable and that spirit of adventure which many of his colleagues and students have found so infectious.

Of all retired men perhaps the retired teacher is happiest. He has the continual joy of learning of or from his pupils and of knowing that they are carrying his ideas and influence to regions where he could never himself have gone. Those who know him will hope that that enjoyment and satisfaction will be his for yet a long time to come.

Nova et Vetera

TRUSS DESIGNED BY LOCKE

John Locke bequeathed his papers to his cousin Peter King, afterwards Lord King, from whom they descended to the Earl of Lovelace. This collection of manuscripts, which was acquired by the Bodleian Library in 1947, reveals the varied nature of Locke's medical interests.

Among them is the paper design of a truss, "to be made in sole leather," a photograph of which is reproduced below by kind permission of Bodley's Librarian. The model is undated, but other correspondence suggests it was designed about 1700. A key to the model, and instructions for fitting the truss, are inscribed across the left-hand flap in Locke's handwriting. It read as follows:

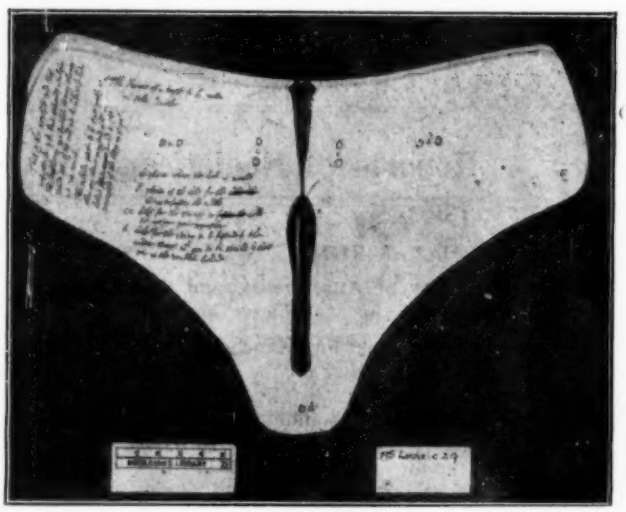
"a place where the hook is notched.
"b place of the holes for the string to fasten the girdle.
"cc holes for the string to hold the upper part together.
"d hole for the string to be fastened to the under straps which are to be strained by hooks set in the doublet behind."

Across the top left-hand corner of the model is written:

"This and the opposite end that answers it, to be bent outwards whilst the leather is moist that it may always stand soe; and the end at d likewise but not soe much.

"The middle part to be bent gently the other way that it may stand with a hollow suited to the convexity of the body in that part."

John Locke was educated at Westminster School and Christ Church, Oxford. He studied philosophy, lectured on moral philosophy and Greek, and had some intentions of taking holy orders. He was elected F.R.S. in 1668. He began to practise medicine with a college friend, but did not take the M.B. degree until 1674; he never graduated M.D. He became attached to the family of his patron Ashley (afterwards first Earl of Shaftesbury) in 1667 and about this time formed a close friendship with Thomas Sydenham. So far as possible Ashley prevented Locke from practising outside his family, by whom Locke was treated as a valued friend.



Being exposed (although unjustly) to the suspicion of complicity in Shaftesbury's political intrigues, Locke left England in 1683 and remained on the Continent until the abdication of James II. On his return he published his *Essay Concerning Human Understanding*, 1690, upon which he had been occupied for 20 years. The *Essay* laid the foundation of modern psychology and established Locke as the leading philosopher of the time. He made no important contribution to purely medical literature, though reference to a projected medical work is to be found in the Shaftesbury papers.

KENNETH DEWHURST.

REFERENCE
MS. Locke, c. 29, fol. 121.

Correspondence

Back to the Barber's Pole

SIR,—A recent circular from the Ministry of Health (12/55/236) describes pre-operative out-patient clinics conducted by anaesthetists. It can be summarized by saying that a patient, seen and recommended for admission by a surgeon, should be referred to a special out-patient session conducted by anaesthetists. At this clinic the anaesthetist examines the patient to see if he is fit for operation, decides when he shall be admitted, carries out special tests, arranges for breathing exercises, dental extractions, treatment for anaemia and obesity, and, whilst seeking the co-operation of the pathology, radiology, and physiotherapy departments, may, in doubtful cases, seek the help of the physician.

Most surgeons would agree that careful pre-operative preparation of patients is a most important part of their daily work, and that it is better, economically, that this should be done before the patient enters hospital. If, in some places, this is not being done, there is an argument for directing the Minister's attention to the improvement of out-patient clinics, and also perhaps for a further review of the training of the surgeon by the Royal College of Surgeons. A pre-operative visit to the patient by the anaesthetist, together with consultation between surgeon and anaesthetist, should be the final steps in making the patient safe for surgery.

This system is very nearly perfect in its proper sharing of responsibility, under the ultimate direction of the surgeon who recommends the operation and who holds the confidence of his patient. Where the system breaks down is where the surgeon and anaesthetist do not fulfil their proper roles; it is a personal failure and not a fault of the system. It cannot be improved by altering the system, but only by choosing and training better people.

What right have we to recommend an operation to a patient who is not fit for operation? How much confidence will a patient feel in a surgeon who advises without careful assessment an operation if, after this and at another clinic, an anaesthetist gives some contrary directions? When we consider the effort that has been needed to give surgery its present high standing in medicine, it seems to be a betrayal of the past and a sacrifice of the future to throw off our responsibility in this way, for in so doing we take the first step back to where we started—shaving and bleeding the patient.—I am, etc.,

Leeds, 6. P. R. ALLISON.

Domiciliary Dental Extractions for Children

SIR,—It has always been a problem to anaesthetize a child under 5 in a dental chair, which with some children is almost impossible unless violence is used. To alleviate the child's anxiety and the mother's fears, and to obviate the mental shock which might lead to psychological disturbances in the child, we have decided to perform suitable dental extractions at the children's homes.

We devised the following technique. We instruct the mother to give the child, about two hours before the appointed time, 1 gr. (65 mg.) of elixir "nembutal" (pentobarbitone) if the child is about 4–5 years of age, or proportionately less or more according to age. By the time we arrive at the house we find the child either fast asleep or awake but in a completely carefree state, showing no signs of fright. When everything is ready the anaesthetic is usually induced by about 5 ml. of ethyl chloride, and then A.C.E. (alcohol 1, chloroform 2, ether 3) is administered by the open method, which we find most convenient and efficient. A sufficiently deep anaesthetic is produced very quickly under these circumstances, and the dental extractions are done. We wait until the child has almost recovered, when we leave the child to the care of the mother.

The extra expense of these domiciliary visits to the N.H.S. only amounts to a fee of 7s. 6d. to the dental surgeon, as the doctor's fees remain the same as if he attended the dentist's surgery. There does not seem to be any objection to this procedure from the Dental Board. From the dental point of view this technique is only resorted to where it is obvious that the child is unsuitable for N_2O, either through being too small or uncooperative, or where there is a gross multiple untreatable caries and/or infection. We have now done over 60 cases during the past few years and we have had no ill effects whatsoever.—We are, etc.,

HERBERT W. SWANN.
Richmond, Surrey. LAWRENCE B. WEEKS.

Engineering and Industrial Hygiene

SIR,—Professor Philip Drinker in his interesting article (*Journal*, June 12, p. 1337) draws attention to a most important difference between the U.S.A. and this country. In America employers have to pay compensation awarded for industrial injuries. To cover themselves they have by law to insure. If the number of claims against any firm is high the insurance company can raise the premium repeatedly. The company has thus a very direct incentive to improve conditions in every way possible. In this country the only fear is an infrequent common law action.

Most doctors in industrial practice must know of firms where year after year numerous accidents and cases of industrial dermatitis occur, most of which could be avoided by institution of preventive measures. The State pays sickness benefit and industrial compensation arising from their neglect. My own experience of industrial dermatitis in particular has for some years led me to wish that an arrangement of insurance and responsibility similar to that in the U.S.A. existed over here. I believe it would do more than anything else to encourage firms to improve their hygiene arrangements.—I am, etc.,

Farnham Royal, Bucks. M. E. M. HERFORD.

General Practice in America and Great Britain

SIR,—"There is great interest and stimulation for the general practitioner [in the U.S.A.] to investigate and treat his patients with a full range of diagnostic and therapeutic facilities, such as is available here [in Great Britain] only to the hospital specialist."

The above statement in the article by Dr. Charles M. Fleming (*Journal*, June 19, p. 1391) seems to indicate some lack of familiarity with the present state of the National Health Service in England and Wales. The "full range" of diagnostic facilities presumably refers in large measure to those offered by the clinical pathological laboratory. With the development of the service in clinical pathology of the regional hospitals I believe it to be the case that there is now no part of England and Wales in which these facilities are not readily available to the general practitioner. It is open to any general practitioner to submit specimens from his patients to the nearest regional hospital laboratory, where they will be examined without charge to himself or to his patient; in those cases where, as is very usual in England and Wales, the regional hospital pathologist works on a part-time basis his services are available to the general practitioner for domiciliary consultations, also without charge to himself or to his patient. The full range of diagnostic laboratory procedures is just as freely open to the general practitioner as to the "hospital specialist."

On the face of it I find it difficult to believe that the position of the general practitioner in England and Wales in respect of laboratory examinations for his patients is in any way less favourable than that of his opposite number in the U.S.A.

The position is, I believe, somewhat different in Scotland, where until lately the policy of the "open door" to the hospital pathological laboratory may not have gained general acceptance and where I believe that no appointment corresponding to that of regional hospital pathologist is held on a part-time basis.—I am, etc.,

Wolverhampton. S. C. DYKE.

Biopsy in Perforated Gastric Ulcer

SIR,—There is one aspect of the problem of the treatment of perforated peptic ulcers which has not, I feel, received the attention that it merits.

Some six years ago I sutured a perforated gastric ulcer in a woman of 29. She was dead four months later of multiple metastases originating from the carcinomatous ulcer that I had sutured. Since that time, in every case of perforation of the stomach which occurs on or proximal to the pylorus, a biopsy has been taken of the whole thickness of the ulcer by two radial incisions extending outward from the hole. In 57 of such cases, 6 have been reported by the pathologist as carcinoma, and gastrectomy within 10 days has been successfully performed. During this period there have also been 2 cases which have been quite obviously perforated carcinoma, and an immediate resection has been done. On no occasion has there been any untoward result of removing a portion of the ulcer for microscopic examination.

Drs. F. Avery Jones and R. Doll in a survey of the late results of perforated ulcer (*Journal*, January 17, 1953, p. 122) found that in 74 patients with perforated "gastric" ulcer 8 subsequently died of gastric carcinoma. I purposely make no reference to the question of late malignant change in gastric ulcers. This would complicate the issue without benefit.

The conclusion which must be reached from my small series and those of Avery Jones and Doll is that one patient in ten suffering from perforated gastric ulcer may well be suffering from perforated gastric carcinoma. If one can be sure that the perforation is in the duodenum, conservative treatment has obviously a great place, but how often can we be sure? May I therefore put a strong plea for a biopsy to be taken in every case of perforated ulcer of the stomach, even when naked-eye appearances give rise to no suspicion that the ulcer is other than benign?—I am, etc.,

Maidstone, Kent. B. E. CRAWFORD STANLEY.

Prophylactic Penicillin for Minor Casualties

SIR,—This week a patient brought me the following letter from a house-surgeon.

"Re A, aged 50. This patient came into casualty Sunday morning having fallen 6 feet (1.8 m.) sustaining minor lacerations to left leg, right hand, and a 1½ in. (3.7 cm.) laceration of the right ear lobe extending a little way into the meatus. No unconsciousness and no headache or vomiting, but he appeared slightly shocked. *X*-ray of skull showed no fracture. The laceration was sutured and he was given A.T.S. 1,500 units procaine penicillin 600,000. As it would be somewhat inconvenient for him to attend casualty each day to finish the course of penicillin I should be glad if you could give it to him. He will be attending us in five days for removal of stitches."

Does the medical profession as a whole believe that such prophylactic injections of penicillin are right and wise? Or that a patient should return to hospital—over 2½ miles (4 km.) away when his doctor is within ½ mile (0.8 km.)—to have stitches removed? I should be glad of the views of others.—I am, etc.,

Kent. G. C. MILNER.

The Male Climacteric

SIR,—I would like to express my agreement with the broad outlines propounded by my friend Dr. A. W. Spence in support of the existence of the male climacteric (*Journal*, June 12, p. 1353). Although many still regard the conception of the male climacteric with prudent scepticism, my views were sufficiently positive in 1948 to permit me to insert a separate chapter in *Major Endocrine Disorders*[1] on the male climacteric, but I ended this chapter with the following cautionary note: ". . . it would be foolish to assume that testicular atrophy is more than one manifestation of old age, or that it is either the cause or the main mechanism of senile degeneration." Further, in a paper given to the Medical Society of London in 1949 on "Impotence"[2] I again reviewed the evidence in favour of the existence of the male climacteric with special references to declining potency and urinary symptoms; but at the same time drew attention to the dangers of giving large doses of testosterone to older people, particularly from the point of view of aggravating existing myocardial insufficiency and bearing in mind that old people may have multiple pathological lesions possibly undetected during life.

Some years previous to this I was a member of a therapeutic trials committee of the Medical Research Council, the object of which was to investigate the alleged beneficial effect of testosterone on benign prostatic enlargement in a large series of cases using both testosterone and inert oil injections, the nature of which was unknown to the observers until after the reports. It was not found possible to produce any objective evidence in favour of a beneficial effect of testosterone, although the evidence was suggestive of subjective amelioration. The trials were based on a presumed relative deficiency of testosterone secretion or relative increase in the oestrogen/testosterone ratio, bearing in mind the effect of oestrogens on the prostate of rats and dogs. Although the tests were negative, or inconclusive, I believe the subject is not unworthy of further investigation. In contrast, the adverse effect of testosterone on malignant prostatic enlargement and the beneficial effect of removing any endogenous testosterone stimulus is well known.—I am, etc.,

London, W.1. S. LEONARD SIMPSON.

REFERENCES

1 *Major Endocrine Disorders*, 1948. Oxford University Press, London.
2 *British Medical Journal*, 1950, **1**, 692.

SIR,—The interesting article by Dr. A. W. Spence (*Journal*, June 12, p. 1353), "The Male Climacteric: Is It an Entity?" cites various references, the earliest date of any of them being 1944.

In June, 1936, I published my book *Change of Life in Men and Women*[1]—written at a time when the idea was a novel one and had not yet entered medical consciousness. Therein I set out the problem and, I think, clearly established the male climacteric as an entity. Though the idea was then odious to many medical men, the book received good medical and other reviews and wide support, and is now in its fourth edition. Would it not have been just to have cited this book in the list of references?—I am, etc.,

London, W.1. MARIE C. STOPES.

REFERENCE

1 *Change of Life in Men and Women*, 1936. Putnam, London.

Tropical Diseases in Britain

SIR,—I should like to join issue with Professor A. W. Woodruff, who, in his article on tropical medicine in Great Britain (*Journal*, May 1, p. 1030), expresses strong disagreement with the idea of diagnosing chronic amoebic dysentery by sigmoidoscopy, in particular dismissing the "pin-point crater" as merely a normal anatomical structure. He deplores the "publicity" which has been given to these lesions—surely the term "publicity" as applied to reports in scientific journals and textbooks is a trifle unusual. It seems that one perhaps significant bit of publicity has escaped his notice—namely, my paper describing the minute anatomy of these lesions.[1] Biopsy shows them to be very far removed from merely gland orifices; indeed, each crater is a miniature flask-shaped ulcer, as can be seen in the photomicrograph illustrating my paper.

My own observations on these lesions extend over the past 10 years and include some 5,000 sigmoidoscopies in India and about 3,000 in returned Service men and others in England. The presumptive evidence for their being the "hall-mark of chronic amoebic dysentery"[2] is as follows: (1) They are very frequently seen in patients whose stools have in the recent past been positive for *E. histolytica*. (2) In serial sigmoidoscopies metamorphosis can be watched, the amoebic ulcers being replaced under therapy by pin-point craters in days or weeks. (3) Cases of chronic bowel disturbance or hepatitis with tropical histories very frequently present these lesions; after anti-amoebic treatment they usually disappear *pari passu* with the symptoms

of the patient, and a relapse is almost invariably accompanied by a recrudescence of the lesions.

This striking parallelism between lesions and symptoms in many scores of patients is most convincing, and appears to me to justify the assumption of their amoebic origin as a practical working hypothesis. This assumption has resulted in the relief of symptoms in so many patients that it cannot be lightly dismissed.—I am, etc.,

Worcester. C. F. J. CROPPER.

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[1] *J. trop. Med. Hyg.*, 1951, **54**, 71.
[2] Cropper, C. F. J. (1945). *Lancet*, **2**, 460.

Aged Sick and Infirm

SIR,—Your interesting leading article (*Journal*, June 19, p. 1425) on the "Aged Sick and Infirm" left me with the impression that we are still meddling with the elderly. One wonders how long it will be before we get to real grips with the problem. Medical neglect of the aged sick is still conspicuous, and will continue to menace all endeavours for their betterment until doctors and hospitals develop new attitudes and think in terms of function rather than the pathology of degeneration.

Domiciliary visiting before admission of the patient is the most important part of the geriatric service given at my unit, and I have been disturbed by the number of patients one sees who have been discharged from general hospitals where very little has been done for them in the way of rehabilitation.

These medicated survivals are becoming an additional burden to all concerned and reflect little credit on the hospital service. Additional beds as suggested is not the answer. What is wanted is better use of present beds, less therapy tinged with despair, and a deeper appreciation by the profession not only of the diseases of old age but of the diseases in old age.—I am, etc.,

London, E.11. J. DELARGY.

SIR,—I should like to express the warm appreciation of the National Corporation for the Care of Old People at the views expressed in your leading article (*Journal*, June 19, p. 1425) in which great emphasis was laid on the importance of keeping old people in their own homes by the provision of various domiciliary services. Similar belief prompted the governors of the Corporation to initiate in Andover, Hampshire, an experiment designed to discover the needs of old people and the use and availability of domiciliary services provided by voluntary and statutory bodies in the area.

May I venture, however, to correct a mis-statement in the article, in which you say that in the homes for the infirm aged started by the Corporation the patients remain for up to eight weeks. In fact, all patients, after assessment at a geriatric unit, are admitted to the home, where they remain, so long as the condition of their health dictates, under the general supervision of the geriatric physician. When fit to leave they are discharged to their own homes if circumstances permit, to local authority communal homes where suitable, or back to hospital if their health deteriorates. Those who waver on the borderline between health and sickness—that arbitrary line which divides the responsibility of the hospital from that of the local authority—and who have no relatives able to take care of them can remain in the home indefinitely. Maintenance costs of patients in the home are met either by the hospital board or by the appropriate local authority after a medical assessment to determine where the responsibility lies, or even by the patients themselves in certain circumstances. If only short-term patients were admitted great care would have to be exercised in their selection to ensure that there was somewhere for them to go at the end of the period. This would preclude many from being admitted who would otherwise have benefited from the less rigid atmosphere of the home.—I am, etc.,

M. R. F. SIMSON,
Secretary,
London, N.W.1. National Corporation for the Care of Old People.

Undergraduate Education

SIR,—Much has been written and spoken in recent years on this subject. It would appear reasonable to assume that some constructive efforts are being made to improve the teaching and training of the undergraduate to qualify him to deal with the common complaints and minor maladies encountered in everyday general practice. May the letters of Dr. Aleck Bourne (*Journal*, June 5, p. 1321) and Mr. W. S. Hanna (*Journal*, June 19, p. 1438) be timely reminders to those responsible that there is still room for improvement.

It will take time for enlightened views to be absorbed and longer still, it is feared, for them to be put into practice; yet there is one single fundamental doctrine—namely, the training of the senses—which appears to receive less attention than it deserves, and its implementation requires neither new rules, new regulations, nor an altered curriculum. To overlook this simple yet fundamental precept in the practice of the art of medicine is to deny the doctor and his patient help which can ill afford to be ignored. Sherlock Holmes may be out of date in this more elaborate and less leisurely age, yet it is relevant to recall that his success was in no small measure founded on close observation—he used his "senses." Let our undergraduates be taught to use theirs.—I am, etc.,

Tunbridge Wells, Kent. R. PROSPER LISTON.

Women in Medicine

SIR,—I would like to point out that a woman medical graduate may gain experience by taking different resident appointments and a postgraduate diploma and also have considerable experience in general practice. After this, if she marries, she is still in a position to continue in her previous work.

It appears to be the attitude of many that a married woman doctor must spend all her time looking after her family. Marriage alone should not debar her from working in the field of her choice. At present she is not even given the chance to prove her capabilities; the fact that she is married prevents her from even being considered. One would think her personal family experience together with professional knowledge would make her a valuable co-worker. In the public health field and in general practice it is quite workable to have a full-time job (with locums at the occasional times of maternity leave), and we all know both surgical and medical consultants who have successfully combined work and family affairs.—I am, etc.,

Brigg, Lincs. MARY HELMER.

"Sulpenin" Therapy Complicated by Oliguria

SIR,—Two cases of sulphonamide anuria have already been described by Mr. J. G. Callanan (*Journal*, January 16, p. 138) and Mr. Howard Jamison (*Journal*, February 27, p. 519). A further case which responded immediately to ureteric catheterization is reported. This case may perhaps again bring to notice the fact that combinations of drugs should be used with care and are not less toxic, in most instances, than their individual constituents. A dangerous attitude of complacency and feeling of safety in the use of polychemotherapeutic agents can perhaps be remedied by the noting of these instances when they arise. Due thought should be given before therapy with multiple agents. In most cases a single chemotherapeutic agent is cheaper, as effective, and more easily controlled. Statistics have been brought to prove combinations are better, and vice versa, but in many cases these should be treated with reserve unless produced on large comparable series and under strict methods of control as in the Medical Research Council trials.

Five days before admission a man aged 68 years had been given "sulpenin" (penicillin, sulphadiazine, and sulphamerazine) for right-sided pleurisy. Approximately 40 tablets were given over three days, when he developed pain in the loins and oliguria. Only a few bloody drops of urine were passed in the two days before admission, when his blood

urea was 180 mg.%. Cystoscopy (Mr. R. P. Smyth) showed general oedema of the bladder and blockage of both ureters. On the left the obstruction was 1 cm. up. On the right crystals could be seen blocking the orifice. Catheterization of each ureter was followed by a flow of debris and crystals with a gush of urine. The catheters were left *in situ* and removed in 24 hours. Potassium citrate was given by mouth and no difficulty was experienced after cystoscopy. His recovery was rapid and uneventful, and he was discharged after one week with a normal blood urea and urinary output.—I am, etc.,

Belfast. ALAN P. GRANT.

Case of Fatal Pyrimethamine Poisoning

SIR,—The case reported by Dr. R. Y. Taylor (*Journal*, August 1, 1953, p. 703) calls to mind the following case that occurred here.

A child, female, aged 3 years was admitted to hospital three-quarters of an hour after swallowing an estimated 25 tablets of pyrimethamine. The stomach was immediately washed out, but approximately 20 minutes later convulsions and unconsciousness developed. The convulsions were only partially controlled by inhalational anaesthesia (chloroform followed by ether, nitrous oxide, and oxygen) and no improvement occurred. The heart remained in good condition until near the end, when it rapidly failed. She died about three hours after the tablets had been taken. The brain and parts of certain organs were submitted to the Government chemist, Nairobi, who reported: "The brain, weighing 1,053 g., was extracted and 17 mg. of base recovered. The remaining small pieces of various organs were bulked and extracted. From the extract a further 14 mg. of base was recovered. As I know of no simple specific test for 'daraprim' the base recovered has not been proved to be daraprim, but it resembles daraprim base in appearance."

While the tastelessness of pyrimethamine makes it particularly suitable for children, a warning should be issued to parents to keep the bottle well out of their reach.—I am, etc.,

Eldoret, Kenya. H. L. PEAKE.

Aldosterone

SIR,—Your leading article on aldosterone (*Journal*, June 5, p. 1311) underlines its property of sodium retention, and, in emphasizing it, appears not to stress certain of its other effects on the metabolism of sodium, included in your data, which may yet emerge as of greater significance. Recent obstetric research may help in this assessment.

Preliminary reference must be made to the researches of Gaudino and Levitt,[1] who found that deoxycorticosterone acetate (D.C.A.), administered to normal dogs, produced expansion of the extracellular space at the expense of the intracellular—the intracellular concentration of sodium and potassium being elevated at the peak of the response. Administration of cortical extract led conversely to expansion of the intracellular space and total body water, and with no alteration in the extracellular space. A like conflicting effect is equally discernible in the experiments you quote, wherein aldosterone was administered subsequent to D.C.A. in the test causing an *increase* in the urine volume and a transient *rise* in the urinary sodium and chloride, possibly to be explained as an attempt to rid the body of sodium chloride and water stored away under the influence of D.C.A.

It is unlikely that the salt-retaining hormone is primarily responsible for the retention of NaCl and H_2O in such diverse conditions as congestive heart failure, nephrosis, and hepatic cirrhosis with ascites, for there appears to be no common aetiological factor to provide the stimulus for its outpouring. To add to the confusion Venning, Singer, and Simpson[2] have just shown an increase in the sodium-retaining factor in the urine of late toxaemia—more marked in the severer types of the disease. The presence of the hormone would find a readier explanation in these clinical conditions if its effects on the distribution of sodium and water were regarded as its major purpose.

Observations further derived from toxaemic investigation would also support this view. Dieckmann[3] has stressed the ominous significance of developing haemoconcentration in impending eclampsia, whilst Lambiotte-Escoffier, Moore, and Taylor[4] have adduced evidence that there is an increased tissue content of water and sodium in pre-eclampsia, though the extracellular fluid content is unaltered, thus bringing their findings into line with Gaudino and Levitt's effect of corticoid extract administration, and possibly accounting for haemoconcentration by the relative increase in red blood cell size. You also provide another explanation by steroid intervention for the production of haemoconcentration when you state that the effects of aldosterone include an increase in the haemoglobin concentration and in the blood non-protein nitrogen *representing the disappearance of the hydraemia* (which develops in the adrenalectomized dog treated with D.C.A.).

It will be realized that the adrenalectomized dog, nurtured on saline, has been used to show the salt-retaining effect of aldosterone. The validity of this method of assessing the properties of an adrenal steroid should be considered along with Prunty's[5] statement: "Only recently have studies commenced to determine the effects on renal excretion of water and electrolytes in response to expansion of extracellular volume *a basic requirement* [my italics] in evaluating the response to cortical hormones." This requirement does not appear to have been satisfied in most of the described tests with aldosterone. However, when salt depots have been created by D.C.A. exhibition, no longer was retention but loss of sodium and water evident on its use—an occurrence supporting the importance of Prunty's thesis.

Aldosterone, from the foregoing, may well prove to be a salt-regulating rather than a pure salt-retaining hormone, especially as in its varied clinical association potassium loss, a characteristic accompaniment of its sodium-retaining action, has not been shown to occur.—I am, etc.,

London, W.1. JOHN SOPHIAN.

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1. *J. clin. Invest.*, 1949, **28**, 1487.
2. *Amer. J. Obstet. Gynec.*, 1954, **67**, 542.
3. *Toxaemias of Pregnancy*, 1952, 2nd ed. Mosby, St. Louis.
4. *Amer. J. Obstet. Gynec.*, 1953, **66**, 18.
5. Second International Congress of Internal Medicine (London) Abstracts, 1952, pp. 12 and 13.

Prolonging the Effects of Drugs Administered by Mouth

SIR,—At the meeting of the Société de Médecine in Paris on May 28 I took part in a symposium on recent advances in therapeutics, when I described experiments on methods of prolonging the effect of drugs administered by mouth. Details will be published in due course, but, pending this, a preliminary report may be of interest. The main difficulty was to find an excipient which would permit immediate absorption of some of the dose but which would spread the absorption of the remainder over a prolonged period of time. Several substances were tried, but ultimately polyvinyl acetate was found to meet the needs. Various proportions of P.V.A. and aspirin were tried. Ultimately long-acting tablets were obtained by combining "free" aspirin with portions of aspirin intimately associated with P.V.A. When 15 gr. (1 g.) of this type of tablet are given, the blood level of salicylate rises to 12 mg.% at the end of an hour, 16 mg.% at the end of four hours, and at the end of twelve hours is still above 3 mg.%. This prolongation of absorption led me to try the effect of a loading dose of 20 gr. (1.3 g.) followed by 15 gr. (1 g.) every twelve hours, and by this means it was possible to maintain indefinitely a level which did not fall below 15 mg.%. Individual variations are remarkably slight.

I tried a similar combination of procaine penicillin and P.V.A. and obtained prolongation of the same type; thus, twelve hours after giving 1 mega the blood level was 0.6 unit per ml. I then gave ½ mega, and twelve hours later the blood level was the same, although in the interval it had risen as high as 0.9 unit per ml. This level could be maintained indefinitely by 12-hourly doses of ½ mega. These penicillin tablets have been given to just over one hundred people with practically identical results. The only case in which there was relatively poor absorption was one of chronic sprue. I tried similar experiments with sodium *para*-amino-salicylate and the results have been of the same type—that is, maintenance of adequate blood levels for periods of over 12 hours. Mice have been given polyvinyl acetate in their food for many weeks and no signs of absorption or toxicity have been detected.

One great disadvantage of oral medication has been the necessity for frequent administration if a continuous effect

was required. My results appear to indicate that this difficulty has now been overcome. An adequate blood level can be maintained for over twelve hours by giving the usual dose in the form of these long-acting tablets, whereas the same dose, unprotected by P.V.A., would be effective for four to six hours only.

Messrs. Arthur H. Cox & Co. Ltd., of Brighton, have not only provided numerous experimental preparations, but have also made available their research data concerned with continuous absorption from enteric "depots." I am grateful to Continental Laboratories Ltd. for supplying the definitive products.—I am, etc.,

London, E.13. A. PINEY.

Acetone Tests in Diabetic Coma

SIR,—We are indebted to Dr. K. J. Gurling and Mr. H. R. Millar for having tried our acetone test using 2,4-dinitrophenylhydrazine (*Journal*, May 15, p. 1154). As far as we can see, they have only looked for "colour change or crystal formation" in the D.N.P.H. reagent proper; but, as this often proves negative, we advised (*Journal*, April 3, p. 816) a subsequent vigorous shaking with equal volumes of carbon tetrachloride (preferably guaranteed reagent). If very small amounts of acetone are present an additional shaking with 5 N sodium hydroxide is advisable. If this procedure had been followed, we feel certain that Dr. Gurling and Mr. Millar would have reached different results.

In order to prove this point we first tried the Nessler reagent advocated with aqueous solutions of acetone. The reagent was found to be at least as sensitive as our D.N.P.H. reagent (which shows the presence of 0.008–0.01 mg. of acetone). Whereas the positive D.N.P.H. reaction is immediate, the positive Nessler reaction for small amounts of acetone takes some minutes to develop. In order to compare the "binding capacity" of the respective reagents, we rigged up an "artificial patient" so as to obtain controlled volumes of "expired air." A suction pump with a constant flow of water of 1,400 ml./60 sec. carried air through water with 0.05% acetone and then carried this acetoneous air through 20 ml. of one of the reagents. A fresh acetone solution was used at each experiment. By repeated tests we found an illustrative, reproducible case where 45 seconds of running time immediately gave a faint but distinctly positive D.N.P.H. reaction by the previously described extraction method, whereas the Nessler reagent became faintly opaque after 30 minutes—that is, 1,800 seconds—which is a long time to wait.

We have not found it necessary to test for tobacco smoke, but acetaldehyde is a source of error in both reactions. The "aspiration trap" advocated and depicted seems very simple and practical, but is not strictly necessary with our reagent and procedure. Finally, we do not entirely agree with the statement that "tests for acetone in the breath may be of help, but they are far less important than examination of the urine." In 25 diabetic patients with suspected light ketosis and showing positive reactions to the D.N.P.H. test in exhaled air, we found some few with negative Gerhardt's and Legal's reactions in the urine.—We are, etc.,

R. DYBKÆR.
O. SYLVEST.

Copenhagen.

Coloured Driving-glasses

SIR,—Referring to your annotation (*Journal*, June 5, p. 1313), headlight dazzle may be minimized by wearing one of the cheap tinted sunglasses with celluloid "lenses" from which all but the temporal portion of the right lens and the nasal portion of the left lens has been cut out with scissors. Minor trimmings are made by experiment in the stationary car against an object on the near off-side, a trifle more lens being removed from the left lens. Deep tints may be used. The central and near-side vision is unimpaired and the off-side vision is not impaired more than it would be by naked dazzle.—I am, etc.,

Merthyr Tydfil. E. ASLETT.

Leucoplakia

SIR,—The following case may be of some interest to readers.

A man aged 45, who was number one trumpet player in a travelling orchestra, consulted me on account of pain in the upper lip which was making it extremely difficult for him to play correctly. He stated that for the first half-hour of a performance he would not notice very much pain, but after that it was difficult to carry on, and he saw his livelihood as a musician coming to an end. On examination there was a small white film obvious on the mucous membrane in the centre of the upper lip. He had had ointments previously prescribed in New Zealand without obtaining benefit from them. My diagnosis was that it was a leucoplakia. I decided to desiccate the area by diathermy, using a fine spark from the end of a needle electrode. Fortunately, immediately after this he contracted influenza and was confined to bed for a few days, but following that he found playing was extremely difficult owing to some swelling and pain, and he had to resort to the position of second trumpet player. It was with difficulty that he was able to continue in this role. While the company was returning to Australia he was asked to play on board ship, after not having played for a period of five days. He decided to do so with some trepidation, but to his great delight found that he was able to go through the whole performance without any trouble. This occurred exactly six weeks from the date of desiccation.

I saw this man again two years later and there had been no further recurrence of his trouble, and he is now playing first trumpet with another company, which entails a very heavy programme of work.—I am, etc.,

Christchurch, N.Z. W. GORDON RICH.

Acute Post-operative Laryngeal Obstruction

SIR,—In the article "Acute Post-operative Laryngeal Obstruction" by Mr. J. B. Prendiville and Dr. H. G. Middleton (*Journal*, May 15, p. 1126), the authors describe four children who suffered from the condition. Two of the patients were intubated with rubber tubes and two with "flexometallic" tubes, the latter tubes having, I believe, a rubber covering. The flexometallic tubes were No. 1, but the size of the rubber tubes used was not mentioned; 10% cinchocaine ointment was the lubricant in all cases. The method of sterilization of the tubes, the length of the operations, and the flow of gases were not mentioned.

My experience indicates that the following factors are important in minimizing respiratory complications, particularly in children: (1) Use plastic "portex" tubes in all cases. These tubes are non-allergenic, whereas some individuals are sensitive to rubber. (2) Use too small rather than too large a tube in children, and if, necessary, assist the respirations. (3) If the flow of gases approaches or exceeds the minute volume they must be humidified to avoid drying of the mucous membrane of the tracheo-bronchial tree. This applies particularly in long cases. (4) Sterilize endotracheal tubes by boiling and keep "surgically clean." This has no ill effect on the "portex" tubes. Soaking the tubes in antiseptic solutions, even if thoroughly rinsed before use, can lead to trouble. (5) Never use a stylet to stiffen the tube—that is, with children; trauma can result. (6) Use sterile liquid petrolatum as the lubricant. It can be poured on and the excess shaken off. The business end of the tube does not need to be handled and the lubricant remains sterile for further use. Only a slight film remains in the tube, certainly not enough to cause "oil pneumonia." Analgesic agents are unnecessary in the lubricant. If the tube is not moved there is no irritation, and if it is moved the local analgesia is of no avail in any case. Water-soluble lubricants contain tragacanth, which is well known for its allergenic properties.

Before appreciating the above points some of my colleagues and I had our share of trouble. We tried soaking the tubes in aqueous benzalkonium chloride ("zephiran") 1/1,000 at one time, and had several cases of post-operative stridor. I had a case of laryngeal oedema in an asthmatic woman after using a water-soluble jelly as the lubricant.

A 4-year-old boy required a tracheotomy after using a rubber tube, which was also on the large side. There has been no serious trouble of this kind in my practice since adhering to the above six criteria—that is, for several years. May I express my satisfaction that this problem is being aired at last? The authors deserve credit for bringing up the matter.—I am, etc.,

New Westminster, British Columbia. F. A. WALTON.

Foreign Bodies in the Lungs

SIR,—On the north wall of the chancel of the church of St. Mary, Plympton, is a marble tablet to the memory of Henry Villiers Parker, Viscount Borringdon, who died at St. Mandé, near Paris, on November 1, 1817, aged 11 years and 5 months. The monument bears the signature and date "F. N. Delaistre, 1819," and shows two putti leaning against an obelisk wth a portrait medallion of the boy. The following is part of the inscription:

"His death was occasioned by having on the preceding 21st July incautiously taken into his mouth an ear of rye which passed into the windpipe and was found after its fatal effects were completed entire and unchanged in the substance of the lowermost parts of the lungs. The illness which ensued was supported with a firmness, cheerfulness and patience which circumstances the most trying could never disturb."

—I am, etc.,

Coffinswell, Devon. WYNDHAM E. B. LLOYD.

Carotinaemia

SIR,—The following case of carotinaemia may be of interest.

A female infant of 8 months was seen by us on April 22, 1954, as the mother thought the child was jaundiced. On physical examination the infant appeared alert and of normal size and weight for birthweight of 7 lb. (3.2 kg.). The skin was a bright lemon-yellow colour, most pronounced in face, hands, and feet. The sclera were normal in colour. The liver edge only was palpable, and there were no other abnormal physical signs.

The diagnosis appeared to be carotinaemia, and on discussing the child's diet the mother told us that she had been giving about half a pound (0.2 kg.) of carrots in purée form at lunch each day since the child was weaned two months previously. Pathological investigations on April 23, 1954, were as follows: (*a*) icteric index, 7 units; (*b*) van den Bergh—direct and indirect—negative.

The mother was advised to omit carrots from the diet for a few weeks, and when last seen by us on May 18, 1954, the colour of the child's skin had reverted to normal. We would like to thank Dr. J. Keall for the pathological investigations.—We are, etc.,

R. G. B. WIGODER.
H. G. JEFFS.

London, S.E.6.

Occupational Bladder Tumours

SIR,—Recently published observations of Walpole, Williams, and Roberts[1] on the induction of tumours of the urinary bladders of dogs by the oral administration of 4-aminodiphenyl (para-aminodiphenyl or "xenylamine") have an important bearing on a paper entitled "Tumour of the Urinary Bladder as an Occupational Disease in the Rubber Industry in England and Wales."[2] This paper claimed that there appeared to be an occupational risk of developing bladder tumour attached to work in compounding, moulding, extruding, and vulcanizing rubber, and it was suggested that this risk was introduced with and perhaps caused by a certain antioxidant made from α- and β-naphthylamine. Certain brands of this antioxidant were found to contain a small proportion (about 2%) of unreacted amine. It was explicitly stated that the evidence produced was not proof of this hypothesis, since the scanty data available could not exclude other substances being causal agents.

In discussing the various classes of antioxidants used it was stated: "Two only, on our present knowledge (i.e., in 1949), might be regarded as possibly being able to give rise to a potential bladder tumour hazard." Both of these substances were based on α-naphthylamine or on α- and β-naphthylamine, and the use of at least one has been abandoned and existing stocks destroyed.

The findings of Walpole and others referred to above make this statement incomplete and possibly misleading, since a publication[3] of the *India Rubber World* in 1942 listed at least one antioxidant which is based on 4-aminodiphenyl. What the position is at the moment as to use I do not know, but evidently antioxidants based on this substance must be added to the list of suspected materials. Furthermore, this extension of the list should make one suspicious that not all classes of dangerous compounds have been detected. It is therefore clear, whether antioxidants based on 4-aminodiphenyl have been used or made in this country or not, that the question of bladder tumour as an occupational disease in the rubber industry in England and Wales merits further investigation.—I am, etc.,

Chester Beatty Research Institute, Royal Cancer Hospital, London. ROBERT A. M. CASE.

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1 *Brit. J. industr. Med.*, 1954, **11**, 105.
2 Case, R. A. M., and Hosker, Marjorie E. (1954). *Brit. J. prev. soc. Med.*, **8**, 39.
3 *Compounding Ingredients for Rubber*, 1942, 2nd edition. Compiled by the Editors of the *India Rubber World*. New York.

Domiciliary Obstetrics

SIR,—It was a pleasure to read Dr. Ivor Cookson's article on domiciliary obstetrics (*Journal*, April 10, p. 841). I recently published a similar survey dealing with 500 home deliveries.[1] Our cases were delivered by fifth-year medical students as part of their training in obstetrics in this institution. Pre-natal clinics were run by the students under my supervision. Each student is accompanied by a qualified midwife during the course of a labour, and I am on call at all times for complications or emergencies.

During the three-year period February, 1951, to December, 1953, our service conducted 500 deliveries at home. In addition, 113 cases were referred to hospital for delivery. Our indications for hospital delivery are essentially the same as those presented by Dr. Cookson. Even though the majority of our cases were delivered under very poor home conditions, often on the floor and usually without proper lighting, our results as summarized below in table form appear quite satisfactory. We use no anaesthetics except pethidine and occasional whiffs of trichlorethylene.

Results in 500 Home Deliveries

	No. of Cases	Percentage
Toxaemia	22	4·4
Tears of perineum:		
Primiparae	26	23·6 of primiparae
Multiparae	17	4·4 of multiparae
Episiotomy	15	3·0
Forceps (low)	2	0·4
Premature labour	10	2
Intra- or post-partum haemorrhage	11	2·2
Stillbirths	8	1·6
Neonatal deaths	4	0·8
Erythroblastosis	0	0
Puerperal morbidity	13	2·6

In summary, our findings confirm the conclusions of Dr. Cookson that domiciliary obstetrics is safe provided patients are under constant supervision by qualified medical personnel during pregnancy and labour.—I am, etc.,

American University Hospitals, Beirut, Lebanon. ALEX KOUYOUMDJIAN.

REFERENCE

1 *J. méd. Liban.*, 1954, **7**, 98.

Pernicious Anaemia

SIR,—I would ask to be permitted to answer the criticism of my letter (*Journal*, April 24, p. 983) made by Dr. R. P. Goulden (*Journal*, May 29, p. 1264).

First, I would mention that my clinical diagnosis of pernicious anaemia is made only when the following symptoms are found: a severe macrocytic anaemia, a megaloblastic response in the bone marrow, a slightly raised serum bilirubin and absence of gastric abnormalities as shown by *x* ray following a barium meal, and a histamine-fast achlorhydria. I do not consider finding a minute amount of acid in my patient after an histamine injection significant. The

possibility of malnutrition or malabsorption is constantly kept in mind, and, as reported in my letter, these conditions were excluded by a fat analysis of the stools, including a fat balance test, which were both within normal limits on the two occasions that the patient was admitted into hospital. The patient had no absorptive difficulties.

Secondly, I would add that my object in studying and publishing these cases of Addisonian pernicious anaemia refractory to the parenteral administration of refined or crude liver extract or vitamin B_{12} is to establish that they exist and to elicit reports from other haematologists. For Dr. Goulden to suggest that this patient was not suffering from Addisonian pernicious anaemia because she did not respond to vitamin B_{12} suggests that this condition always responds to this vitamin. It has been shown that there are cases which require a total liver preparation such as proteolysed liver for adequate response and maintenance.[1 2 3 4]

To conclude, it is my experience that these refractory cases show no evidence whatever of the sprue syndrome, and I am satisfied that this patient was, in fact, a case of megaloblastic anaemia indistinguishable from Addisonian pernicious anaemia, resistant to refined and crude liver and vitamin B_{12} by injection but responsive to proteolysed liver by mouth.—I am, etc.,

Birmingham, 18. R. O. GILLHESPY.

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2 Goldsmith, G. A. (1951). *Proceedings of the Third International Congress of the International Society of Haematology*, p. 11. New York.
3 Beard, M. F. (1950). *Lancet*, **2**, 407.
4 Gillhespy, R. O. (1953). *Practitioner*, **171**, 648.

Single Incision for Bilateral Orchidectomy

SIR,—Mr. C. J. Cellan-Jones (*Journal*, May 1, p. 1039) expresses dismay at Sir Heneage Ogilvie's advocacy (*Journal*, April 17, p. 934) of a scrotal approach to the testis, and he hopes that young surgeons will not be tempted to apply the technique to spermatocele, hydrocele, etc. I write in respect of hydrocele only.

It is not difficult to understand why Mr. Cellan-Jones in the bitterness of experience abandoned the scrotal approach, and I can also understand why Sir Heneage Ogilvie abandoned the cumbersome inguinal approach. Indeed, working in an area where the prevalance of hydrocele is due to bilharzia and filariasis and where imperfect technique invites disaster, I have largely abandoned both textbook methods.

The dangers of the orthodox scrotal approach are: (1) oozing from the extensive peeled area despite meticulous haemostasis; (2) lymphatic and venous stasis due to the coliapse and retraction of the empty scrotum; (3) the size of the wound necessary for delivering the hydrocele and the extreme difficulty of coapting satisfactorily the scrotal skin edges in their collapsed and wrinkled state; (4) the drain so often deemed necessary.

All four factors which lower resistance to sepsis can be obviated by the following method. An incision 1½ in. (3.8 cm.) in length is made in the scrotum, exposing the tunica vaginalis, which is separated digitally from the overlying layers until a pocket large enough to accommodate the testis has been excavated. The hydrocele is evacuated and incised sufficiently to permit delivery of the testis through the opening in the tunica and the wound. As the testis is drawn out the tunica is turned inside out and anchored in this position by one suture. The testis can now be slipped back into the pocket initially made for it, and fits snugly enough to exert haemostatic pressure. It will now be found that the scrotal skin overlying the testis is stretched just sufficiently to smooth out the wrinkles, that the tendency of the edges to curl inwards has ceased, and that two or three sutures coapt the edges with a gentle tension and no tendency to gape. There is virtually no oozing. A corridor of skin extending from the wound to the inguinal region with undisturbed lymph drainage is obtained, and the combination creates a resistance which overcomes the risk of infection from the undoubtedly unsterile skin.

In my experience the bulk of the redundant tunica is less than the bulk of clotted blood and serum which would result from stripping and excising it, and in the 200 patients on whom I have used the method convalescence has been most rapid and complications almost non-existent.—I am, etc.,

Busia, Uganda. GORDON CURRIE.

Medical Hypnosis

SIR,—Medical uses of hypnosis as an adjunct to other methods of therapy, from the induction of relaxation, analgesia, or even deep anaesthesia for surgical operations, to its employment in reducing the somatic accompaniments of emotional tension and the effects of hysterical syndromes, have been known for years. Yet acceptance of the potential value of this most interesting phenomenon has always been complicated by the air of mystery or even of occultism with which it has been surrounded. Even to-day a critical evaluation of the therapeutic possibilities of hypnosis in various fields of medicine has yet to be attempted.

The proper employment of hypnosis as a therapeutic weapon must depend upon humility and objectivity in assessment of results, combined with an experimental attitude towards the clinical problems involved. The undersigned are interested in exploring the uses of hypnotism and hypnotherapy in all branches of medicine and surgery, with a view to obtaining an evaluation of the method by experts and practitioners in every relevant field. To this end we would invite doctors interested in planning objective research and discussing different methods and techniques to contact Dr. Gordon Ambrose, at 62, Queen Anne Street, W.1.—We are, etc.,

WILLIAM MOODY. C. M. GWILLIM.
D. STAFFORD-CLARK. J. CRAMOND.
GEORGE NEWBOLD. GORDON AMBROSE.
E. E. WOOKEY.

London, W.1.

Rose Simmonds Memorial Fund

SIR,—In December, 1952, an appeal was sent to you by the British Dietetic Association for publication in your *Journal* (December 13, 1952, p. 1318) for contributions to the above fund. The object of the appeal was to provide an educational fund which, through the British Dietetic Association, would be able to offer scholarships to students to train as dietitians, or prizes to students in training.

The Trustees of this educational fund wish it to be known that a sum of £370 has been contributed. This money has been invested, and the trustees have decided that the first prizes to students will be available in the autumn of 1955.—We are, etc.,

DOROTHY S. RUSSELL. W. R. S. RITCHIE.
H. G. WIMBUSH. E. P. SKINNER,
Chairman, British Dietetic Association.
E. M. GAGE,
London, S.W.3. Honorary Treasurer, British Dietetic Association.

POINTS FROM LETTERS

Herpes Zoster and Chicken-pox

Mr. W. C. J. COOPER (Lovedale, C.P., S. Africa) writes: The letter from Dr. C. Spencer Whitehouse (*Journal*, May 8, p. 878) prompts me to record a similar experience. A few weeks ago our son, aged 10, developed a typical chicken-pox eruption on the anterior and posterior aspects of the lower half of the trunk. Two days later an eruption typical of herpes zoster developed on the right upper half of the trunk. Each eruption followed the course normally to be expected of the condition with which it is associated. It was most interesting to observe these two different eruptions simultaneously on the one individual.

B.M.A. Coat of Arms

Dr. W. Z. SMITH (London, W.C.1) writes: With reference to the proposed coat of arms for the B.M.A. described by Dr. S. F. Logan Dahne (*Journal*, June 26, p. 1491), surely the circulation could be represented as a figure of eight, but never conceivably as a circle.

Obituary

SERGEI SERGEVITCH YUDIN, Hon.F.R.C.S., Hon.F.A.C.S.

Professor Sergei Sergevitch Yudin, director of surgery at the Sklifassovsky Institute for Traumatic Diseases at Moscow, died suddenly in Moscow on June 14. He was a great surgeon, and his reputation spread far beyond the boundaries of the U.S.S.R. Besides being an honorary Fellow of the Royal College of Surgeons of England he also held the honorary Fellowship of the American College of Surgeons. Among the honours conferred on him by his own country were the Order of the Red Star and the Order of Stalin. We are greatly indebted to Sir GORDON GORDON-TAYLOR for the following appreciation:

Those who were members of the Anglo-American Surgical Mission to Russia in 1943 during the second world war will experience a sense of personal loss in the death of Sergei Sergevitch Yudin; but surgeons everywhere will also mourn the passing of one whose reputation was international. Yudin was born in 1891. After four years in the medical school of Moscow University he joined the Russian Army in 1914 and was wounded three times in the first world war, one of these injuries involving the spine and producing a paralysis which confined him to bed for nine months. After the October Revolution (1917), organized by Lenin and Trotsky, and its aftermath had withdrawn Russia from the conflict, Yudin, working at the Zakharino Hospital, actively interested himself in the study of extensive thoracoplasty for chronic pleural empyema. For this work he was made a member of the Russian Surgical Association. In 1922 began his surgical sojourn at the Industrial Institute, Serpouhoff, and during this period he paid special attention to the problems of anaesthesia. After flirting for a time with infiltration of the solar plexus according to the technique of Braun, he produced a monograph on spinal anaesthesia. In 1926 he visited the Mayo Clinic and also the clinics of Crile, Cushing, and Babcock in the United States. In 1928 he was appointed to the famous Sklifassovsky Institute in Moscow.

In 1932 he visited Spain, France, and England, and he honoured me with a visit to my operating theatre at the Middlesex Hospital. A book from his pen on "Transfusion of Corpse Blood" was published by Masson et Cie, of Paris, about this time. He was the only Russian surgeon who ever journeyed beyond the frontiers of that huge land, and he eagerly acquainted himself with recent work and innovations of technique emanating from workers in other countries: he was profoundly interested in the Marriott–Kekwick technique of "drip-transfusion," and in turn Kekwick visited Yudin just before the war to study corpse-blood transfusion.

The record of his achievements indicates the range of his surgical activities: thus nearly 5,000 foreign bodies were removed from the oesophagus and air passages by Yudin and his assistants between 1928 and 1942. By 1943, when our Military Mission visited him, he had fully completed 89 cases of oesophagoplasty, with the infinitesimal mortality of two: and in a letter to me, written in 1947, he informed me that the number had risen to almost 150. He was a staunch advocate of the employment of a segment of small intestine brought up in front of the sternum to replace the impermeable oesophagus; and he preferred to "by-pass" the stomach at the abdominal termination of the new food-tube, and the intestinal oesophagus was inserted en-Y into the jejunum.

In 1943 Yudin's experiences in gastric surgery had amounted to over 5,000 operations performed in the preceding 25 years. His experience of acute perforated peptic ulcer comprised over 2,000 cases: he had performed over 100 total gastrectomies, including one such operation on his own mother, who was alive in 1943, having survived the operation more than five years. In 1943 he had performed 281 gastro-duodenal resections for ulcer haemorrhage. His technique of pushing the duodenal stump closed *en escargot* into the ulcer crater in the pancreas is a useful surgical manœuvre for the control of haemorrhage from the ulcer base. A paper by Professor Yudin entitled "Treatment of Gunshot Fractures of the Limbs" was published in this *Journal* in 1943 (November 6, p. 567).

On s'a demandé longtemps si Yudin vive, for the finely woven mesh of the Iron Curtain permits little news to trickle through: anxious hope had long bandied questions with despair. But a recent number of *Medicinski Rabotnik* ("Medical Worker") has put an end to uncertainty, announcing his sudden demise—he had a coronary thrombosis in 1942—and specifying the awards and orders which had been bestowed upon the distinguished surgeon by his country. But he was very proud himself of the honorary Fellowship of the Royal College of Surgeons of England which was conferred upon him in Moscow in 1943, and the Commissar of Health graciously gave his permission for Yudin to be photographed alongside Elliott Cutler and me in his Fellowship gown.

Yudin was adored by his staff at the Sklifassovsky Institute, as may be seen in the beautiful appreciation of him by his former first assistant, Petrov, in the *Festschrift* number of the *Annals of the Sklifassovsky Institute* on the occasion of Yudin's fiftieth birthday: he refers to him throughout as "S.S." (Sergei Sergevitch). He was the outstanding Russian surgeon of his day: he realized that the science and art of surgery could be advanced only by contacts with workers in other countries, and he travelled abroad on occasion, although he was not permitted to be accompanied by his wife. He was of the surgical stature of men like Pirogoff, Oppel, or Federov: he had organizing abilities of the first order and a dynamic energy which drove him relentlessly, especially during the early period of the last great war, when his assistants left him to serve with the armed forces and he worked almost single-handed and wrote feverishly war manuals and bulletins for the instruction of those launched on a new field of surgical practice. Even when the inevitable coronary thrombosis laid him low, his activity scarcely abated, but his supreme moment came when in June, 1942, he was appointed a consulting surgeon at the front in the uniform of the famous Red Army. His personality was captivating: he was a poet, writer, fisherman, dilettante, lover of all things beautiful, perfervid patriot. It is good to have known "S. S."

C. C. HOLMAN, M.B., F.R.C.S.

Mr. C. C. Holman, formerly senior surgeon at the Northampton General Hospital, died at Dodford, Northamptonshire, on June 17 at the age of 69.

Charles Colgate Holman was born at East Hoathly, Sussex, on September 18, 1884, the son of the late Dr. Thomas E. Holman, and was educated at Eastbourne College, where he won an open scholarship to Gonville and Caius College, Cambridge, in 1903. Receiving his clinical training at Guy's Hospital, he qualified M.R.C.S., L.R.C.P. in 1908, taking the M.B., B.Chir. degrees in the following year and the F.R.C.S. in 1912. After holding a resident post at Guy's and similar appointments at hospitals in the provinces, he became house-surgeon at Northampton General Hospital in 1912. During the first world war he served in the R.A.M.C. and on demobilization returned to Northampton, where he was appointed assistant surgeon to the General Hospital in 1919 and surgeon in 1925. He was senior surgeon of the hospital from 1926 until his retirement in 1952, when

the title of emeritus surgeon was conferred upon him. He was also consulting surgeon to the Kettering General Hospital from 1943 to 1952. For many years he served on the board of management and the house committee of the Northampton General Hospital, and he was chairman of the medical staff committee.

Though a general surgeon, Mr. Holman had a special interest in fracture and orthopaedic work and became the first surgeon to the Manfield Orthopaedic Hospital, Northampton, in 1925; he was also surgeon to the children's orthopaedic clinic in the town. A past president of the Northampton Medical Society, he was also president of the Northamptonshire Branch of the B.M.A. in 1933 and again in 1947. For recreation, Mr. Holman was keen on bridge and on tennis, which he continued to play with competence and enjoyment until well into his sixties, despite the handicap of a limp caused by an attack of poliomyelitis at the age of 21. He was twice married. His first wife, formerly Miss V. E. Fowell, died in 1921 leaving two sons, the elder of whom is a doctor. In 1923 he married Miss Violet Lewis, and she survives him.

We are indebted to Dr. E. E. T. TAYLOR for the following appreciation: Charles Holman lived for his work, and no man ever gave more painstaking and kindly personal attention to his patients. The care and wide knowledge he showed in the wards were matched by his sound technique in the operating theatre. Difficulties only stimulated his persistent energy, for he maintained the avid interest of the student to the end of his life, being invariably well informed on current literature, contributing a number of articles himself to the medical journals. During the last war he undertook the care of all fractures treated at the Northampton General Hospital and personally operated on every compound fracture admitted during that time, in addition to carrying out his full share of the routine and emergency work as a general surgeon. He had an original turn of mind, and had devised and practised for years some newly described techniques, such as an abdominal approach to femoral hernia and a method of suprapubic puncture. He also designed special instruments for the insertion of Smith-Petersen pins. He ensured that an adequate staff should meet the increasing needs of Northampton General Hospital, even though it meant handing over work in which he had much interest. His integrity was absolute, and in all his dealings no thought of personal advantage ever crossed his mind. Holman was of a naturally quiet disposition and intimately known only to a few friends, yet among those with whom and for whom he worked he commanded profound respect and an inevitable affection. His death has been sorely felt.

Dr. F. F. WADDY writes: Mr. C. C. Holman worked in Northampton as a general surgeon from the close of the first world war until his death. He was peculiarly shy and rather over-reluctant to talk to patients and relatives, apparently fearful to say anything which might be construed as drawing attention to himself and his surgery. Occasionally this characteristic puzzled new patients, though those who knew him placed an implicit confidence in his clinical judgment and surgical skill.

He was perhaps the most versatile surgeon in England. Being the first surgeon to specialize in surgery in Northampton to the exclusion of general practice, he was called on in the early days to act as gynaecologist, obstetrician, and orthopaedic as well as general surgeon. His aim in life was to serve his patients and increase the status of the hospital in which he worked, so that when a gynaecologist and obstetrician was appointed he willingly gave up the work and unselfishly referred hospital and private cases alike to his new colleague. During the war he took on all the fracture work at the General Hospital, and this in turn he handed over when the time came. There is no doubt that he did this with the deepest regret, but again he would not allow his own personal desires to interfere with the progress and expansion of the hospital.

I anaesthetized for him for nearly 25 years, and never saw him as anything but the perfect gentleman at the operating table. Knotty problems he would discuss in detail with infinite patience. Considering the vast amount of work he did, his promptitude was amazing and his courtesy unending. Over all these years junior anaesthetists repeatedly requested to be allowed "to give anaesthetics for Mr. Holman because they gained confidence working for him."

E. J. BOOME, M.B., M.R.C.P., D.P.H.

The sudden death of Dr. E. J. Boome on June 12 was a sad blow to his many friends and colleagues. He was consultant in speech therapy to the London County Council and retired a few years ago from the post of principal assistant medical officer to the council.

Edward James Boome was born on May 20, 1883, and was educated at King Edward School, Birmingham, and at Birmingham University, where he graduated M.B., Ch.B. in 1907. After holding resident posts at the General Hospital and Queen's Hospital, Birmingham, he took the D.P.H. in 1912. Before joining the service of the London County Council in 1913 as assistant in the school medical service he was an assistant medical officer under the Surrey County Council for two years. In the first world war he served overseas with distinction, reaching the rank of major and being mentioned in dispatches. A member of the Territorial Army since 1911, the Territorial Decoration was conferred on him in 1925. In the service of the L.C.C. his work was over the whole field of school medicine. He was expert in the diagnosis and ascertainment of backward and crippled children and for a time was medical officer to the council's Farmfield Institution for Mental Defectives and lecturer to the nursing staff there. In 1934 he was admitted M.R.C.P.

A pioneer in the study of speech defects, Dr. Boome was largely responsible for the development and teaching of speech therapy in the L.C.C. service and eventually became consultant to the council. He was a founder member of the College of Speech Therapists and the author of several standard textbooks. He was also a member of the Board of Registration of Medical Auxiliaries, the British Council for Rehabilitation, and the Research Board for the Correlation of Medical Science to Physical Education.

Since his official retirement in 1948 he had carried on working part-time in the staff medical examination section of the L.C.C.'s health department. He had done this work for many years, and his clinical ability and courteous charm earned him respect and affection. He will be greatly missed and long remembered, and the sympathy of all his colleagues goes out to his widow.

F. B. writes: Dr. E. J. Boome's medical work in the hopfields was of great value and interest, but he will be chiefly remembered for his work on speech therapy. At a time when there were many vague ideas on stammering but little clear thought or logical treatment, he brought common sense to bear on the problem. This can be seen in his two books *Relaxation in Everyday Life* and *Abnormal Speech*—both becoming classics and gaining for his methods of therapy acceptance not only in England but in America and many other countries. He was responsible for founding the speech centres of the L.C.C. which for the first time alleviated the unhappiness of the large numbers of stammering children and adults of a large city. But his real

contribution to medicine was the humanity and kindness with which he treated patients whom he saw in his official capacity, thus not only demonstrating to the public that medicine can still be human though "official," but also teaching the generations of young public health doctors who worked under him that medicine is greater than bureaucracy, that duty is always to the individual patient and not to the machine.

RAGHAVENDRA ROW, O.B.E., M.D., D.Sc.

The news reached us recently of the death at his home at Bombay of Dr. Raghavendra Row on November 14, 1953, two days before his 82nd birthday.

Raghavendra Row was born in the North Kanara district of Bombay on November 16, 1871. After qualifying L.M.S. at the Grant Medical College in 1893 he held the post of Mayo demonstrator in physiology at the College before entering University College, London, as a postgraduate student. Later he continued his medical studies at University College Hospital Medical School and graduated M.D. from London University in 1898. Six years later he obtained the London D.Sc. He was the Grocers' Company's research scholar for 1898–9. After taking his London degrees Dr. Row returned to Bombay, where he established himself in consultant practice. In due course he became senior physician to the J. J. Hospital and consulting physician to the Gokuldas Hospital, Bombay, and visiting physician and bacteriologist to the B. D. Petit Parsee General Hospital. Throughout his long life he possessed the inquiring mind of the perpetual student and in other circumstances might have become a research worker of the first rank. Though lacking the opportunity and the facilities to devote his whole time to research he was not prevented from gathering clinical material which, in the intervals between the work of his private practice, he studied in his own private laboratory.

Dr. Row was appointed professor of medicine at the Grant Medical College in 1921, and from 1926 to 1931, when he retired, he was professor of pathology there. He vacated the chair of pathology with the knowledge that he had not only organized the department to his own satisfaction but had seen it properly housed and equipped. After his retirement from the College he worked out a scheme of research for the Lady Tata Memorial Trust, and was closely associated with the opening of the P. G. Singhani Hospital, of which he was an honorary director and honorary consulting physician. At the time of his death he was a vice-chairman of the board of trustees and a member of the management committee of the Bombay Hospital.

During the whole of the first world war Dr. Row served as an honorary medical officer and senior physician at the Lady Hardinge War Hospital, Bombay, with the rank of lieutenant-colonel in the I.M.S. For his war services he was mentioned in dispatches and in 1920 he was appointed O.B.E. He was also awarded the Kaisar-i-Hind gold medal in 1912; the Lord Minto gold medal for research in 1921; and the Barclay medal of the Asiatic Society of Bengal in 1934 for his valuable contributions in the realm of biological sciences.

A member of the British Medical Association for 54 years, Dr. Row served as a vice-president of the Section of Tropical Medicine at the London Meeting in 1910. He was also president of the Bombay Branch from 1926 to 1928 and acting honorary secretary of the Branch in 1926. He represented his constituency at the Annual Representative Meetings of 1910, 1924, and 1932.

A prolific writer on a wide variety of subjects, including leishmaniasis, malaria, rat-bite fever, leprosy, plague, enteric fever, he had a number of communications published in this *Journal* between the years 1902 and 1924.

Edinburgh men of his time will be distressed to learn of the sudden death on June 3 of Dr. A. J. M. BUTTER at his home in North London at the age of 59. Andrew James Moyes Butter was born on November 15, 1894, and at the outbreak of the first world war was in the Faculty of Arts at Edinburgh University. Joining the Royal Engineers, he was soon drafted to France, where he won the Military Medal as a sergeant with the special gas company of that regiment, in which he was later commissioned. After the war he took his M.A. at Edinburgh, and obtained the M.B., Ch.B. in 1923. Those were highly competitive days, when only the very best of the large number of men graduating could hope to secure house appointments, particularly in the teaching hospitals. Butter was among the selected few, and was successively house-physician to Professor Edwin Bramwell at the Royal Infirmary and house-physician at the Royal Hospital for Sick Children, Edinburgh. He came to London, and before entering general practice was house-physician at Queen Mary's Hospital for the East End. He proceeded to the M.D., with commendation, in 1925. J. A. B. Y. writes: Among a number of gifted men prominent in the life of Edinburgh University after the first world war Butter was an outstanding personality. A member of the Students' Representative Council and of the Debating Society, he was also president of the Philomathic Society and, in 1923, president of the University Union. In spite of these public activities he was at heart rather a shy person and certainly never sought the distinctions that came his way. He had a delightful sense of humour, and a gift for public speaking that was not lessened by an appearance of diffidence on rising to his feet. During Butter's year as president of the Union Mr. Lloyd George was installed as Lord Rector of the University. At the subsequent luncheon in the Union speeches were made by the Lord Rector and other great men, but many who heard Butter speak that day felt that he had outshone the others. His facility for the *bon mot* was tested, and found not wanting, in Paris. He acted as guide, philosopher, friend, and spokesman of the Edinburgh party studying midwifery there in 1923 and was an immense favourite with the French students. At social functions Butter always spoke for us—in French—and his remarks were invariably received with acclaim. He was a gifted physician greatly beloved by his patients, among whom were included many of his colleagues and their families. To see him enter the sickroom, so kind, so patient, and so capable, was to have confidence in him. In spite of the demands of his large private practice he found time to be on the staff of the Wood Green and Southgate Hospital and was also medical officer in charge of St. David's Hospital for Epileptics. In the latter appointment he had almost unrivalled experience, and was a great authority on epilepsy, particularly in the drug treatment of the condition, on which he had written a number of valuable papers. Another of his interests was the local medical society, the Ganglion Club, of which he had been secretary for many years. Some three years ago there were the first indications that all was not well with his health, but he continued his full work, and the end, when it came, was unexpected and in the midst of a busy day's work, as he might have wished. No medical man was ever more admired and respected by his colleagues than this gifted and unassuming man, who to the end preserved a remarkably youthful appearance. He was incapable of any action other than a generous one, and his place in the medical community will be hard to fill. He will be sadly missed and will not be forgotten. He leaves a widow, formerly Miss Ena McLaren Laing, who also graduated in medicine at Edinburgh in 1923, and two sons.

Medical Notes in Parliament

Rock Carling Inquiry

Mr. LESLIE LEVER (Manchester, Ardwick, Lab.) asked the Minister of Pensions and National Insurance if he would state the date on which the Rock Carling Committee was appointed; when the committee's report was expected; and what action he proposed to ensure early consideration of the report and implementation of the findings. Brigadier J. G. SMYTH, Parliamentary Secretary, stated on June 24 that the committee was appointed in July, 1950, and made reports in April, 1951, and January, 1953. In the latter report they recommended that further clinical inquiries should be made before final conclusions were reached on the matters submitted to them. Over 5,000 pensioners were accordingly specially examined and the results had been supplied to the committee, who were considering them. The Minister would consider the final report as soon as he received it, but he was not yet in a position to say when it would be available.

Tuberculosis in Wales

Mr. CLEDWYN HUGHES (Anglesey, Lab.) asked the Minister of Health for the figures of the incidence of tuberculosis in England and Wales respectively, and the number of persons suffering from tuberculosis who were awaiting admission to sanatoria in each of the two countries. Mr. IAIN MACLEOD stated on June 21 that in 1953 the number of primary notifications of new cases of tuberculosis (all forms) per million population was 1,041 for England and 1,289 for Wales. On December 31, 1953, the number of persons on clinic registers awaiting admission to sanatoria was 4,322 for England and 660 for Wales.

Mr. GORONWY ROBERTS (Caernarvon, Lab.) asked the Minister on June 24 if he would give the reasons why the number of primary notifications in Wales was much higher in 1953, proportionately to the population, than in England; and Mr. HUGHES asked why the number of persons on clinic registers awaiting admission to sanatoria in Wales was higher than the average for the country as a whole, and what steps he was taking to improve the position. Mr. IAIN MACLEOD replied that there certainly tended to be a higher rate of notification in Wales than in England. He was not aware of any single specific reason to account for this, although it partly accounted for the numbers awaiting admission. In 1953 the number examined by mass radiography increased by 36,000 over 1952, and was about 250,000 yearly. He was constantly watching the position. Beds were already more, *pro rata*, than in England, and everything possible was being done to recruit more staff. Two new thoracic units were already being set up for surgical cases (at Chepstow and Newport).

Foreign Beneficiaries of Health Service

Mr. IAIN MACLEOD, Minister of Health, told Mr. J. MCINNES (Glasgow, Central, Lab.) on June 24 that information was not available about the number of persons not permanently resident in Great Britain who obtained medical and surgical treatment in England and Wales under the Health Service, or of the cost.

Mr. JAMES STUART, Secretary of State for Scotland, gave a fuller answer to a similar question about Scotland. He said no precise information was available, for Health Service patients were not required to provide evidence of their permanent residence. Apart from the provision of drugs, treatment of non-residents by general practitioners involved no extra Exchequer cost, because the aggregate remuneration of general practitioners did not depend on the total number of patients. Special inquiries at particular hospitals in 1950 suggested that not more than one-tenth of 1% of hospital expenditure related to persons from abroad. It could be assumed that the total cost to the Exchequer of treating non-residents under the Health Service did not exceed £50,000 a year in Scotland.

Industrial Benefit.—The preparation of schemes under the Industrial Diseases (Benefit) Act is well advanced, Mr. R. H. TURTON, Parliamentary Secretary to the Ministry of Pensions and National Insurance, stated on June 21, and the Minister hopes soon to consult interested organizations about the detailed proposals.

Reciprocal Security.—Negotiations have been resumed with the New Zealand authorities for a reciprocal agreement on social security, and the Ministry of Pensions and National Insurance discussed the matter personally with Sir William Bodkin, the New Zealand Minister of Social Security, at the end of May, according to a reply by Mr. R. H. TURTON on June 21.

Athlete's Foot Among Miners.—The Minister of Fuel and Power said on June 21 that he had no information about the relative incidence of athlete's foot in mining areas with pithead baths and in other areas, but a committee had been set up recently to inquire and advise on the prevention and treatment of this disease among miners.

More Chemists.—There are 15,622 chemists' shops making up Health Service prescriptions, compared with 14,822 in 1951, according to a reply given by Mr. IAIN MACLEOD on June 24.

Medico-Legal

WRIT OF HABEAS CORPUS

An application to the Divisional Court for leave to issue a writ of habeas corpus addressed to Dr. H. C. Maurice Williams, the medical officer of health of Southampton, and for an order to be made for the immediate release of a patient from the Coldeast Mental Colony was brought last week.[1] The application was made by the father of the patient, a girl who reached the age of 21 on January 10, 1954, and who had been under restraint since the age of 15. At the application on June 22 counsel for the father of the girl said she had been on licence infrequently, but had shown she was well able to take care of herself and earn her own living. The parents had been informed that the case would be reviewed when the girl reached the age of 21. On May 4, 1954, the girl's mother wrote to the Board of Control and was told that "the statutory requirements in regard to the reconsideration of your daughter's case consequent upon her attaining the age of 21 years were not carried out. As a result the Board consider that the order under the Mental Deficiency Acts in respect of her lapsed by operation of law on April 10, 1954." When the girl's mother wrote to the medical officer of health of Southampton asking for her daughter's release, she was told that the M.O.H. had carefully considered her daughter's circumstances and had decided that a fresh petition should be presented to the magistrate, and that meantime a temporary authority was issued legalizing her stay at the colony. When the case was heard on June 25 counsel for the applicant said the girl had been released from the colony the day before and was back with her parents. In the circumstances the petition had been abandoned, but he applied for costs of the application against Dr. Williams. Counsel for Dr. Williams, opposing the application for costs, pointed out that the M.O.H. had never had the custody of the girl. The Coldeast Mental Colony had nothing to do with him. Certain technical mistakes—for which no officials of the Southampton Borough Council were responsible—had occurred. When the reconsideration of the girl's case took place after she reached the age of 21 the Board of Control had taken the view that the reconsideration was a nullity, and the parents had been told that the girl would no longer be detained.

Dr. Williams, said counsel, had acted in all good faith in taking the view that if the girl went home she would be

[1] *The Times*, June 23 and 26, 1954.

neglected, and he had to consider the interests of the girl and of the public. He had thought that the proper procedure would be to present a petition on behalf of the local authority to the magistrates. He took the action which he did under what he considered to be his powers under Section 15 of the Mental Deficiency Act, 1913, which applied where an "officer of the local authority found neglected or abandoned . . . any person who he had reason to believe to be a defective." However, after the proceedings which had taken place in the court on June 22 counsel advised that the girl could not be said to be neglected, and she was then released.

In giving judgment on the question of costs, Mr. Justice Hilbery said: "We accept that he (Dr. Williams) was acting in perfectly good faith, but if something is done in good faith which is wrong I cannot see why people who have to incur legal costs to establish their legal rights should have to pay costs themselves. The proceedings will be withdrawn, subject to an order for costs against the respondent."

Vital Statistics

Week Ending June 19

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 651, whooping-cough 1,970, diphtheria 20, measles 3,106, acute pneumonia 309, acute poliomyelitis 32, dysentery 896, paratyphoid fever 11, and typhoid fever 3.

Infectious Diseases

Infectious diseases were less prevalent in England and Wales during the week ending January 12. The falls in the number of notifications included 303 for whooping-cough, from 1,989 to 1,686; 245 for dysentery, from 1,017 to 772; 82 for acute pneumonia, from 417 to 335; 62 for scarlet fever, from 793 to 731; 33 for measles, from 2,834 to 2,801.

The largest fall in the local trends of whooping-cough was 57 in Lancashire, from 230 to 173. Only small fluctuations were reported in the trends of scarlet fever. 8 cases of diphtheria were notified, 10 fewer than in the preceding week. This is the smallest number ever notified in any week. The largest variations in the incidence of measles were rises of 111 in Lancashire, from 553 to 664; 88 in Yorkshire West Riding, from 224 to 312; and falls of 64 in Yorkshire North Riding, from 173 to 109; 63 in Norfolk, from 253 to 190; and 52 in Staffordshire, from 219 to 167.

8 of the 12 cases of paratyphoid fever were notified in Durham (Gateshead C.B. 3, Blaydon U.D. 4, Washington U.D. 1). 3 of 6 cases of typhoid fever were notified in the London borough of Fulham.

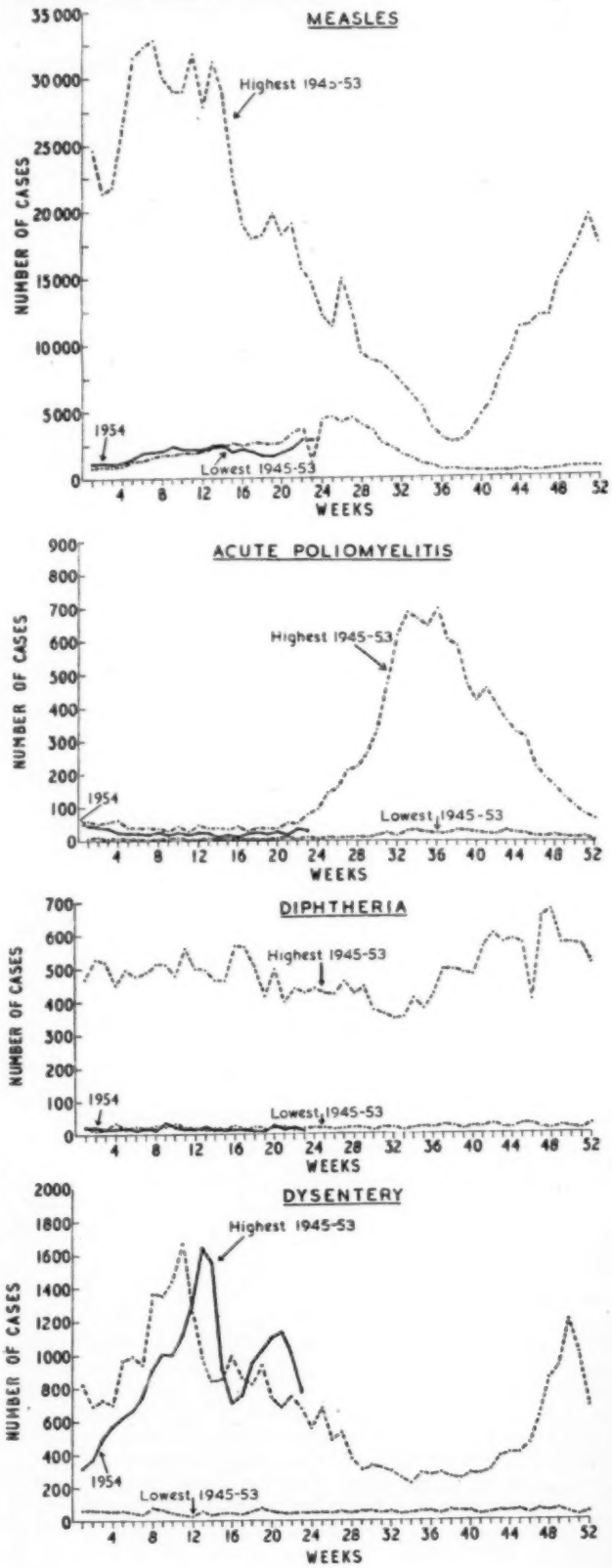
26 cases of acute poliomyelitis were notified during the week, and these cases were 4 fewer for both paralytic and non-paralytic cases than in the preceding week. 3 cases were notified in the counties of Cheshire, Lancashire, and Yorkshire West Riding.

The largest returns of dysentery were Lancashire 180 (Haydock U.D. 44, Liverpool C.B. 17, St. Helens C.B. 17, Bolton C.B. 15, Salford C.B. 12, Farnworth M.B. 12, Kearsley U.D. 10); Yorkshire West Riding 93 (Sheffield C.B. 26, Leeds C.B. 13, Dewsbury C.B. 11); London 71 (Islington 32); Durham 53 (Sedgefield R.D. 20, South Shields C.B. 10); Kent 46 (Penge U.D. 18, Beckenham M.B. 11); Leicestershire 44 (Leicester C.B. 40); Middlesex 38; Staffordshire 37 (Newcastle-under-Lyme M.B. 20); Essex 31; Cheshire 25 (Ellesmere Port U.D. 10); Sussex 24 (Uckfield R.D. 15); Surrey 20 (Croydon C.B. 11).

In Scotland the notifications of dysentery increased from 266 to 281. The largest returns were 198 in Glasgow and 31 in Edinburgh.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1945–53 are shown thus - - - - - -, the figures for 1954 thus ———. Except for the curves showing notifications in 1954, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **June 12** (No. 23) and corresponding week 1953.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	8	0	4	0	0	17	4	7	0	
Dysentery	772	71	281	2	1	486	94	128	3	
Encephalitis, acute	5	0	0	0		5	1	1	0	
Enteric fever:										
Typhoid	6	3	0	1	1	6	1	2	2	
Paratyphoid	12	0	0	0	0	5	1	0	1	
Food-poisoning	197	32		1		241	28		0	
Infective enteritis or diarrhoea under 2 years				9	39				20	14
Measles*	2,801	83	159	265	349	7,532	207	486	259	313
Meningococcal infection	28	3	15	0	2	25	1	14	0	3
Ophthalmia neonatorum	46	4	10	1		40	3	11	0	
Pneumonia†	335	24	138	6	1	366	21	181	5	
Poliomyelitis, acute:										
Paralytic	21	1	6	1	0	51	4	6	3	1
Non-paralytic	5	1				22	1			
Puerperal fever§	222	37	15	1		225	37	8	1	
Scarlet fever	731	45	123	19	35	1,055	64	163	50	57
Tuberculosis:										
Respiratory	669	78	141	48				168	37	
Non-respiratory	108	12	15	8				23	1	
Whooping-cough	1,686	53	266	25	41	3,545	306	576	44	100

DEATHS in Great Towns	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eir
Diphtheria	0	0	0	0	0	0	0	0		0
Dysentery	0	0		0		1	0			
Encephalitis, acute		1			0		1			0
Enteric fever	0	0	0	0		0	0	0		
Infective enteritis or diarrhoea under 2 years	3	0	2	0	1	6	0	4	3	3
Influenza	5	0	0	0	0	5	2	0	0	0
Measles		0	1	0	0		0	0		1
Meningococcal infection		0	0				1	0		
Pneumonia	149	17	10	6	4	163	30	15	10	8
Poliomyelitis, acute	0	0			0	4	0			0
Scarlet fever		0	0	0	0		0	0		0
Tuberculosis:										
Respiratory	77	7	13	1	8	95	14	13	2	4
Non-respiratory		1	16	0	1		3	0	0	2
Whooping-cough	2	0	0	0	0	4	1	0	0	0
Deaths 0–1 year	178	20	27	11	2	235	34	30	7	16
Deaths (excluding stillbirths)	4,456	625	508	109	141	4,636	719	536	96	177
LIVE BIRTHS	7,201	1298	947	242	402	8,424	1134	936	249	488
STILLBIRTHS	186	28	36			203	27	20		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Regius Chair of Midwifery at Glasgow.—The QUEEN has appointed Mr. IAN DONALD to the Regius Chair of Midwifery at Glasgow University in succession to Professor R. A. LENNIE, who retires on September 30. Mr. Donald is reader in obstetrics and gynaecology at the Institute of Obstetrics and Gynaecology, London. He graduated B.A. Capetown in 1930, and then came to St. Thomas's Hospital, London, where he qualified in 1937, proceeding M.D. London and M.R.C.O.G. in 1947. During the war Mr. Donald served with the R.A.F., and in 1953 he was appointed Leverhulme research scholar of the Royal College of Obstetricians and Gynaecologists. He has carried out research on neonatal asphyxia.

West London Medico-Chirurgical Society.—The annual dinner of the 70-year-old West London Medico-Chirurgical Society was held in the Apothecaries' Hall on June 28, with the president, Mr. C. HAMBLEN-THOMAS, F.R.C.S., in the chair. It was attended by many guests, both official and private, the former including the presidents of the Royal College of Physicians and the Royal College of Surgeons, the presidents of the Harveian Society of London and the Chelsea Clinical Society, and a former president of the Hunterian Society. In addition there were Sir WILLIAM MACARTHUR, who had delivered this year's Cavendish Lecture on "Pepys and the Plague" and General SITWELL, who had recently entertained members of the Society at the Tower of London. The theme running through all the speeches was the part that local medical societies have to play in medicine, particularly contemporary medicine with all its bustle, complexity, and excessive paper work. As Sir RUSSELL BRAIN put it when proposing the toast of "The President and the Society," "medical societies are never more valuable than to-day." In making possible the meeting of general practitioner and consultant in easy and informal circumstances the local society exerted an integrative action on medicine. In his reply, Mr. HAMBLEN-THOMAS spoke of the Society's links with the West London Hospital; although local in origin, the Society had proved far from parochial in its influence. The toast of "The Guests and Kindred Societies" was graciously proposed by Mr. ARNOLD WALKER, F.R.C.O.G., and Sir DESMOND MORTON and Sir ARTHUR PORRITT responded. On behalf of the kindred societies, Sir Arthur Porritt said that medical societies gave opportunities for both a genuine professional approach "without lay administration" and genuine friendship among doctors. Finally the president of the West London Medico-Chirurgical Society expressed the thanks of the company to the Master and Wardens of the Apothecaries for the use of their beautiful Hall.

Florence Nightingale Memorial.—A dinner was held at the Mansion House on June 24 to help to raise funds for the Florence Nightingale House. The National Florence Nightingale Memorial Committee of Great Britain and Northern Ireland aims at maintaining this residence for nurses of all nations who have obtained scholarships to carry on their education in London. Contributions to the fund for this purpose should be sent to Lord LUKE, 12, Whitehall, London, S.W.1. After the LORD MAYOR OF LONDON had proposed the loyal toast, Mr. IAIN MACLEOD spoke with sympathy of the aims and objects of the Florence Nightingale House, and, after a response by Lord LUKE, Miss DORA GAFFIKIN, a "Nightingale Nurse," proposed the health of the Lord Mayor and Lady Mayoress. Miss Gaffikin said that the ward of which she was in charge was named the City of London, and most of the beds of that ward had been endowed by the generosity of the livery companies of the city. She went on to say that the link between St. Thomas's Hospital and the City dated as far back as 1552. Florence Nightingale House had been founded as a house for international nursing students

pursuing postgraduate studies in London—a movement which should make for better understanding between nations.

Food Rationing Committee.—With the end of food rationing, the Medical Research Council announces the discharge of its Food Rationing (Special Diets) Advisory Committee. This committee was appointed in 1940, under the chairmanship of Sir EDWARD MELLANBY, F.R.S., the then secretary of the Medical Research Council, at the request of the Health Departments and the Ministry of Food. It was the committee's duty to advise what modifications of the ordinary civilian rations were necessary for invalids. This proved a difficult and often invidious task, which became no easier when after the war ended food rationing was continued. In the mood of the time, people were increasingly intolerant of restrictions of any kind, and it says much for the work of the committee that there was so little complaint about their decisions. In 1949, Sir Edward Mellanby relinquished the chairmanship, and Sir HAROLD (then Professor) HIMSWORTH, who had been the committee's secretary since its inception, became chairman. Others who served on the committee were Professor L. S. P. DAVIDSON, the late Viscount DAWSON OF PENN, Sir FRANCIS FRASER, Lord HORDER, Dr. R. D. LAWRENCE, Professor R. A. MCCANCE, F.R.S., Dr. NORMAN SMITH, the late Sir JAMES SPENCE, and Professor M. L. ROSENHEIM, who was secretary from 1949 onwards.

M.R.C. Fellowships in Clinical Research.—The Medical Research Council has made the following appointments to Fellowships in Clinical Research for the academic year 1954–5: Dr. D. R. COLES (University Department of Medicine, Bristol Royal Infirmary), Dr. VALERIE A. COWIE (Registrar, Maudsley Hospital, London), Dr. E. A. HARRIS (Medical Registrar, Western General Hospital, Edinburgh), Dr. J. G. MURRAY (Surgery Department, University of Aberdeen, and Department of Anatomy, University College, London), and Dr. MARY SMITH (Registrar in Medicine, Royal Infirmary, Glasgow).

International Children's Centre Fellowships.—A number of research fellowships for the academic year 1954–5 are offered to those who wish to work at the laboratories of the International Children's Centre in Paris. The research programme is chiefly concerned with the problems of antituberculosis vaccination and pertussis immunization. The fellowships are at a rate of 60,000 French francs a month. Applications, giving details of education, previous experience, and publications, should be sent together with professional testimonials to Professor L. BUGNARD, International Children's Centre, Château de Longchamp, Paris, 16.

Hospital Beds.—Because the best use of hospital beds has proved one of the most frequently discussed topics at the King's Fund Hospital Administrative Staff College, a study group was formed by the College to collect evidence on the problem. The Group's report is now published under the title "Hospital Bed Occupancy," and frank comments are invited. The report is concerned with the experience of general hospitals in Greater London, the teaching hospitals excepted. It analyses the extent of the problem, its causes, and the reasons for local variation, and then goes on to discuss what administrative economies are possible. The Study Group, under the chairmanship of the Hon. Mrs. A. CAMPBELL-PRESTON, included Sir WILSON JAMESON, two hospital house governors, the secretary of a hospital management committee, a former hospital resident medical officer, and the principal of the Staff College for Ward Sisters. The report is being given a fairly wide free circulation within the hospital service. Copies are obtainable from the King's Fund Hospital Administrative Staff College, 2, Palace Court, London, W.2.

Assistant Editor for "Family Doctor."—Applications from registered medical practitioners are invited for the post of assistant medical editor of *Family Doctor*. Experience of popular medical journalism is essential. A salary of at least £1,500 a year is offered. Further details of the post are given in our advertisement columns on p. 20. The closing date for applications is July 31. *Family Doctor* is edited by Dr. I. HARVEY FLACK.

July "Family Doctor."—The July issue of *Family Doctor* contains the start of a new series, "Letters to Jane." The first is written by Professor W. I. C. MORRIS, professor of obstetrics and gynaecology at Manchester, and deals with conception and early pregnancy. Dr. JOHN W. DUNDEE contributes an article on hypothermia. There are also some topical articles on the care of the skin.

"The Frog."—The recent production of "The Frog" resulted in a profit of £10,000 for the Invalid Children's Aid Association.

B.M.A. Library.—The Library will be closed and the library service suspended from July 30 to August 16 while redecorating is being done.

Dr. D. B. Jelliffe, senior lecturer in paediatrics at the University College of the West Indies, has been appointed W.H.O. Consulting Professor of Paediatrics, All-India Institute of Hygiene and Public Health, Calcutta.

Dr. J. Crossland, lecturer in physiology at St. Andrews University, has been awarded a Commonwealth bursary under the joint Royal Society and Nuffield Foundation scheme. The bursary is to enable him to visit Montreal and work with Dr. K. A. C. ELLIOTT on the behaviour of acetylcholine in the brain.

COMING EVENTS

Western Medicine.—Under the title "Men and Medicine," the first of a group of discussions on the human implications of technical change in under-developed countries, Professor RAYMOND FIRTH, Dr. CHARLES WILCOCKS, and Dr. J. H. F. BROTHERSTON will talk on the Third Programme on Wednesday, July 7, at 8 p.m. (repeated Thursday, July 8, at 6.25 p.m.) on the effects of improvements in public health techniques.

Royal Society of Medicine.—The annual meeting will be held on July 6 at 5 p.m. at 1, Wimpole Street, London, W.1.

Joseph Henry Lecture.—Dr. R. A. M. CASE will speak on "Tumours of the Urinary Bladder as an Occupational Disease" on July 12 at 5 p.m. at the Royal College of Surgeons of England.

Buckston Browne Lecture.—Professor DAVID SLOME will speak on "Experimental Surgery" on July 7 at 5 p.m. at the Royal College of Surgeons of England.

Society for the Study of Fertility.—The annual conference of the society will be held on July 22 and 23 at the Meeting House of the Zoological Society of London, Regent's Park, London, N.W.1. Visitors are welcome and should make application to the secretary, Mr. H. H. FOURACRE BARNS, 31, Weymouth Street, London, W.1, when details of the programme will be forwarded to them.

Nutrition Society.—A symposium will be held at the University College of North Wales, Bangor, on July 23 and 24. The theme of the meeting is "The Efficiency of Food Conversion in Farm Animals." Further information may be obtained from Dr. R. J. L. ALLEN, c/o Monkhouse and Glasscock Ltd., Snowsfields, London, S.E.1.

NEW ISSUES

British Journal of Ophthalmology.—The next issue (Vol. 38, No. 7) will be available in a week's time. The contents include:

PATHOLOGICAL BASIS OF RETROLENTAL FIBROPLASIA. Norman Ashton.
DIRECT OBSERVATION OF THE EFFECT OF OXYGEN ON DEVELOPING VESSELS: PRELIMINARY REPORT. Norman Ashton and Charles Cook.
EFFECT OF OXYGEN ON DEVELOPING RETINAL VESSELS WITH PARTICULAR REFERENCE TO THE PROBLEM OF RETROLENTAL FIBROPLASIA. Norman Ashton, Basil Ward, and Geoffrey Serpell.

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SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Saturday, July 3

BRITISH ASSOCIATION OF ALLERGISTS.—At the Nurses' Home, Leicester Royal Infirmary, 11.10 a.m., Dr. Leslie N. Gay (Johns Hopkins University): Treatment of the Ambulatory Asthmatic with Adrenocorticotropic Hormone; Dr. William Brockbank: Treatment of the Ambulatory Asthmatic with Cortisone. 2.15 p.m., Dr. R. G. Paley: Cutaneous and Other Reactions to Insulin; Dr. R. R. A. Coombs, Dr. J. C. Moffat, and Dr. C. H. Whittle: Antibodies to Egg Albumen in Human Sera; Dr. K. Wilken-Jensen (Copenhagen): Allergy in Children.

Tuesday, July 6

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Professor F. C. Ormerod: Indications for the Use of Antibiotics in Otolaryngology.

●INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. J. P. Martin: Cerebral Thrombophlebitis.

LONDON UNIVERSITY.—At Guy's Hospital Medical School, 5.30 p.m., special university lecture by Professor A. R. McIntyre (University of Nebraska): Some Observations of Electrical Activity in Normal and Pathological Muscles.

Wednesday, July 7

OXFORD UNIVERSITY.—At Radcliffe Infirmary, 5 p.m., Professor Alexander Brown (University College, Ibadan, Nigeria): Medicine in the Tropics.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Air Marshal Sir Harold Whittingham: Some Medical Problems of Aviation.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Buckston Browne Lecture by Professor David Slome: Experimental Surgery.

Thursday, July 8

●INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. P. H. Sandifer: Traumatic Paraplegia (2).

LIVERPOOL MEDICAL INSTITUTION.—Conversazione: Studies in Inheritance. Opener, Dr. C. A. Clarke.

LONDON UNIVERSITY.—At St. Mary's Hospital Medical School, 5.30 p.m., special university lecture by Professor Edward W. Dempsey (Washington University, St. Louis, U.S.A.): Some Problems in Cellular Biology as Studied with the Electron Microscope.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Bertram Louis Abrahams Lecture by Professor E. B. Verney, F.R.S.: Some Aspects of the Renal Excretion of Water and Salt.

Saturday, July 10

INSTITUTE OF ORTHOPAEDICS.—At Brockley Hill, Stanmore, 10 a.m., Mr. H. J. Seddon: Teaching Ward Round.

Monday, July 12

ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—5 p.m., William Guy Memorial Lecture by Dr. Lester R. Cahn (New York): Oral Infections: The Evolution of their Treatment.

APPOINTMENTS

BLAIKLEY, J. B., M.S., F.R.C.S., F.R.C.O.G., Honorary Consultant in Gynaecology to the Queen Alexandra Military Hospital, Millbank, in succession to Mr. Frank Cook, F.R.C.S., F.R.C.O.G., whose tenure of the post has expired.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—D. W. A. Drew, M.R.C.S., L.R.C.P., L.D.S. R.C.S., Anaesthetic Registrar, South Devon and East Cornwall Hospital, Plymouth.

UNITED LEEDS HOSPITALS.—John Michael Winn, M.R.C.P., D.M.R.D., Consultant Part-time Radiologist.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Barrowcliff.—On June 18, 1954, at Warwick, to Germaine (formerly Aquettant), wife of Dr. Derek F. Barrowcliff, a second son.

Gilks.—On May 27, 1954, at St. Mary's Hospital, Paddington, London, W., to Nancy (formerly Franklin), wife of Dr. A. W. Gilks, a brother for Nicholas—Charles Franklin.

Pritchard.—On June 19, 1954, to Drs. Meira (formerly Jones) and T. Gwilym Pritchard, Pen-y-Groes, Caernarvon, a brother for John Morris.

Watkinson.—On June 3, 1954, at The Firs Maternity Hospital, Nottingham, to Peggy (formerly Jones), wife of Dr. J. L. K. Watkinson, of 15, Florence Road, Thorneywood, Nottingham, a son—Timothy Robert.

DEATHS

Hislop.—On June 10, 1954, at the Memorial Hospital, Darlington, Co. Durham, Lawrence Hislop, M.D.

McCloghry.—On June 1, 1954, at Edinburgh, Harriet McCloghry, M.B., Ch.B., D.P.H., of 5, Randolph Place, Edinburgh.

McHattie.—On June 1, 1954, Thomas John Tyndale McHattie, M.D., of "Woodsmoke," Curdridge, Southampton.

Norman.—On May 31, 1954, at Salisbury, Southern Rhodesia, Burford Noel Norman, M.C., M.R.C.S., L.R.C.P.

Roberts.—On June 3, 1954, at Richmond, Surrey, Edmund Cleaton Roberts, M.B., Ch.B., formerly of Bedford, and West Byfleet, Surrey, aged 78.

Ross.—On June 10, 1954, at Nairn, Winifred Margaret Ross, O.B.E., M.B., Ch.B., of Auchendean, Dulnain Bridge, Inverness-shire.

Simmons.—On June 3, 1954, at his home, Fair Oak, Hants, Richard Whetham Allpress Simmons, B.M., B.Ch.

Stanton.—On June 1, 1954, at Tavistock, Devon, James William Wilcocks Stanton, M.R.C.S., L.R.C.P., Surgeon Commander, R.N., retired.

Summerville.—On June 4, 1954, at Brockley, London, S.E., David Summerville, M.B., Ch.B., formerly of Dunfermline.

Thierry.—On June 7, 1954, at University College Hospital, London, W.C., Edward Henry Thierry, M.Sc., M.R.C.S., L.R.C.P.

Thom.—On June 2, 1954, at Edinburgh, Alexander Glen Thom, L.R.C.P.& S.Ed., L.R.F.P.S., L.D.S., of 3, Cluny Avenue, Edinburgh.

Verling-Brown.—On June 3, 1954, at the Royal Masonic Hospital, London, W., Charles Richard Verling-Brown, M.D., D.O.M.S., of "Dalveen," Little Bookham, Surrey, aged 79.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Vaginal Thrush

Q.—*What treatment is recommended for a persistent vaginal thrush in a woman of 30? Gentian violet, "pruvagol," "mycil," acetarsol, Bonney's blue, and triple sulpha cream have all been tried with little success.*

A.—When monilia infection resists ordinary methods of treatment, hyperglycaemia or intermittent glycosuria should be excluded by a glucose tolerance test. The remedies already used may not have been applied regularly or for a sufficiently long period. Alternatively, they themselves may have caused a local reaction; gentian violet is particularly prone to do this. The possibility of reinfection from another site in the body, or from the husband or other member of the household, should be considered.

While the infection is being treated the patient should rest as much as possible and should avoid coitus and intravaginal tampons. Antibiotics and sulphonamides of all kinds should *not* be given either locally or systemically, because they tend to prevent the establishment of a normal vaginal flora. Whichever antiseptic is used intravaginally, it should be applied regularly, twice daily at first and thereafter once daily, and it is most important to continue and intensify treatment during menstruation. Moreover, treatment should not be stopped until at least one month after all signs and symptoms of infection have disappeared. Before each application of any antiseptic it is helpful to douche or swab out the vagina with 1% sodium bicarbonate solution, hydrogen peroxide, or a detergent solution. As regards antiseptics for vaginal application a choice can be made from one of the following: phenyl mercuric nitrate pessaries; "diodoquin" tablets; 1 or 2% aqueous mercurochrome applied as a paint; acriflavine in the form of pessaries or douches of 1 in 1,000 solution; and silver picrate pessaries. Attention to detail as regards method of use is probably more important than the choice of antiseptic.

Squatting for Delivery

Q.—*I have heard that among some more primitive peoples—for example, Eskimos and races of Northern India—women in labour are delivered in a squatting position and that their incidence of perineal lacerations is significantly lower than ours. Is this so? Could it be due to the position, and, if so, why is the squatting position not used by us?*

A.—There is evidence that the squatting, sitting, or kneeling postures were usually adopted for childbirth in various parts of the world thousands of years B.C. They continued to be in general use until comparatively recent times, and they are still used by various primitive peoples and by isolated individuals or groups of individuals in more civilized countries. Indeed, it is not so very long since the birth stool, on which the woman sat or squatted for delivery, disappeared from European obstetric practice.

Squatting is probably the most natural position for childbirth, and it has repeatedly been a subject of correspondence in this journal during recent years. A strong advocate for it in this country has been Dr. Kathleen O. Vaughan, whose book *Safe Childbirth*, Baillière, Tindall and Cox (London, 1937) should be consulted.

One of the several advantages claimed for the squatting position is that it opens the bony outlet and the lower birth canal, thus reducing the number and extent of perineal

tears as well as making delivery easier. When assessing its value in this respect, however, other factors need to be considered. For example, the type of life previously led by the women who practise it may result in supple joints and other tissues; such women may marry and have children at an early age while the perineal skin and muscles are resilient; there may be racial differences in the size of their babies or of their heads.

While the merits of the squatting posture are generally recognized it is nevertheless used only by a few obstetricians in this country. This may be partly because of upbringing and prejudice, but it is also because the position of the woman makes it extremely difficult if not impossible for the attendant to observe progress or to deliver the baby under aseptic conditions. It is more suitable perhaps for the unattended woman. Moreover, even its enthusiastic supporters emphasize that to obtain full benefit from the squatting position the patient must have regularly squatted throughout her life—as do primitive peoples living close to the earth. Set exercises during pregnancy cannot make up for restricted movements and an unnatural existence during the early formative years.

The arguments on both sides are many, and suffice it to say that modern practice is a compromise in that the woman is now kept on her back in an exaggerated lithotomy position for most of the second stage of labour and often for the actual delivery. In other words the thighs are acutely flexed on the trunk as in the squatting posture in order to open the outlet as much as possible and yet leave the attendant free access to the vulva.

Relief of Ascites

Q.—*Is there any danger in drawing off ascitic fluid as rapidly as one can, using a standard-sized needle?*

A.—The answer to this question is, No. The danger that is reputed to accompany rapid withdrawal of ascitic fluid is collapse of the patient, and if the rate of flow is left entirely uncontrolled this is a possibility.

It is not clear what the questioner means by a standard-sized needle, but if he is thinking of a serum needle, 18 S.W.G., the fluid could not be withdrawn through it sufficiently fast to produce collapse even if considerable suction were applied. Most patients prefer to have the procedure completed as rapidly as possible with a trochar and cannula, of 11 S.W.G. or 8 S.W.G., and with one of these 10 pints (6 litres) can safely be withdrawn in 8 or 10 hours. Other patients are less disturbed when a Southey's tube is introduced, but then the fluid loss is very much slower and the end of the tube tends to get blocked with fibrin.

If collapse should occur during this minor operation, apart from giving stimulants, the abdominal binder that should have been placed in position under the patient before the paracentesis was begun can be drawn tight, thus increasing the intra-abdominal pressure and tending to relieve the patient of his symptoms.

Climate and Infantile Eczema

Q.—*One of my patients is a baby of 6 months who has infantile eczema. It is intended that he should go to West Africa in three months' time. What effect does the climate have? Should any special precautions be taken?*

A.—Many subjects of constitutional eczema are better in warm dry climates, but most are aggravated by a hot and humid climate. It is likely that the lowlands and coastal regions of tropical West Africa would be unsuitable for a baby with infantile eczema, but the drier uplands might be satisfactory. The only special precautions should be directed to the avoidance of undue sweating and the wearing of suitable clothing. It must be remembered that vaccination against smallpox carries some slight risk of surface and systemic spread of virus infection, and this can be serious.

Hazards of Dibenzyl Disulphide

Q.—*I would be most grateful for any information you could give me on the hazards (especially in relation to dermatitis) of the use and production in a chemical factory of dibenzyl disulphide.*

A.—Many organic sulphur compounds are notoriously troublesome in respect of both systemic and dermatitic effects in manufacture and in use. Each compound in general requires its own investigation, and no analogical comment is completely satisfactory as a basis on which to lay a conclusion. Inorganic sulphides and polysulphides are also often troublesome, especially in causing dermatitis.

On the whole aliphatic sulphur derivatives are more troublesome than aromatic, and among the latter is dibenzyl disulphide. Dibenzyl disulphide is fairly readily oxidized to dibenzyl disulphoxide, which is probably the basis of its use as a protective additive in certain situations. Much more troublesome than the dibenzyl sulphide itself are the substances from which it is made—for example, benzyl chloride and sodium sulphide; the former is a powerful lacrimator and skin irritant, the latter a skin irritant to which some people are extremely sensitive.

Thus, dibenzyl disulphide as such may be regarded as relatively unlikely to give trouble, but the process of manufacture is potentially hazardous. Nevertheless, it should always be kept in mind that there are subjects whose skin can become intolerant to almost any organic agent, and low melting compounds are notorious in this respect (M.P. of dibenzyl disulphide is 71–72° C.).

Clear Urine Clouds on Standing

Q.—*If a specimen of urine is passed perfectly clear but becomes cloudy on standing for a short time, what is the significance?*

A.—The cloudiness or deposit is due to either amorphous phosphates or amorphous urates. If the latter the deposit or turbidity will disappear on gently warming the urine. If due to phosphates any heating will not remove the turbidity and by driving off carbon dioxide may cause it to increase. Any phosphatic deposit will be readily soluble on the addition of a few drops of 33% acetic acid.

NOTES AND COMMENTS

Prickly Heat.—Dr. D. REID TWEEDIE (Perak, Malaya) writes: I have just returned from long leave in Europe and read the reply by your expert on the subject of prickly heat ("Any Questions?" January 2, p. 54). May I say that the measures recommended are really prophylactic. The most successful and infallible treatment in my long experience is dabbing with a lotion consisting of 1/1,000 mercury perchloride in spirit (rectified, methylated, or industrial). Dermatitis medicamentosa is unlikely because a very few applications suffice—if combined with the prophylaxis mentioned above. It is curious that prickly heat is not nearly so common in Malaya as one would expect.

Infection from the Chalice.—Dr. H. G. ANDERSON (Church Missionary Society, London) writes: I have made detailed inquiries about the outbreak of hydrophobia following Holy Communion described by Dr. Lilias M. Jeffries (*Journal*, May 29, p. 1278), but have found no evidence of a C.M.S. missionary dying at the time and place in question, still less any evidence that one died in the circumstances which Dr. Jeffries reports.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1 TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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